ARMED FORCES EPIDEMIOLOGICAL BOARD

SPRING 2005 MEETING

COHOSTED BY THE
ARMED FORCES MEDICAL INTELLIGENCE CENTER (AFMIC)
AND
THE U.S. ARMY MEDICAL RESEARCH INSTITUTE OF
INFECTIOUS DISEASES (USAMRIID)

DAY ONE -- OPEN SESSION

Dalrymple Conference Room (1425)
The U.S. Army Medical Research Institute of
Infectious Diseases (USAMRIID)
1425 Porter Street
Fort Detrick
Frederick, Maryland

Tuesday, March 22, 2005

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PRESENT:

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John Glen Morris, Jr., M.D., M.P.H.&T.M.
Stephen M. Ostroff, M.D. [President, AFEB]
Michael N. Oxman, M.D.
Michael D. Parkinson, M.D., M.P.H.
Kevin Patrick, M.D., M.S.
Gregory A. Poland, M.D.
David A. Savitz, M.S., Ph.D.
Dennis Shanahan, M.D., M.P.H.
Roger W. Sherwin, M.D.

Roger L. Gibson, Colonel USAF, B.S.C., [AFEB Executive Secretary]

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C O N T E N T S

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P R O C E E D I N G S

(12:43 p.m.)

DR. OSTROFF: With the Board members' indulgence, I'd like to get started a couple of minutes early and start by something which we traditionally do. We have several new members of the Board for which this is their first meeting. Traditionally we ask the new members if they would introduce themselves, give a little information about their backgrounds, so that we can better get to know each other. We do have three new members of the Board who have not previously been here. So I'd like to start by asking each of them as if they would be so kind to introduce themselves.

The first is Dr. Oxman. You do have to use the microphone, so it is better if you sit down.

DR. OXMAN: I'm Mike Oxman. I'm a professor of medicine and pathology at the University of California in San Diego. I'm a virologist and an infectious disease doc, and my mentor was John Enders in Boston and Wally Roe,

who is largely responsible for the military adenovirus vaccines that were so successful in the past, among things. I'm looking forward to getting my official security clearance into the computer so that I can join you.

DR. OSTROFF: Thanks very much. We also have Dr. Savitz.

DR. SAVITZ: I'm David Savitz. I'm a professor and chair of the Department of Epidemiology at the University of North Carolina School of Public Health, with most of my research focused on reproductive and perinatal epidemiology. Also occupational and environmental health.

DR. OSTROFF: Thanks very much. We also have Dr. Sherwin.

DR. SHERWIN: Thank you. I'm Roger Sherwin and I recently retired from Tulane University and now live in Santa Fe. I spent most of my career at the University of Maryland, and my interest is primarily in cardiovascular epidemiology, and my methodological interest is in

clinical trials.

DR. OSTROFF: Thanks very much. Our last new member is Dr. Ananth.

DR. ANANTH: Hi. I'm Cande Ananth and I'm an associate professor of obstetrics and gynecology and the director in the Division of Epidemiology and Biostatistics at the Robert Wood Johnson Medical School and University of Medicine and Dentistry of New Jersey.

DR. OSTROFF: Thank you very much as well.

I talked with Colonel Gibson, and as I mentioned briefly, I did actually put together some comments to mark the fact that this is my last meeting as Board president. Since I know that traditionally a lot of the members of the Board have to leave early the second afternoon, I was just wondering if you would indulge me and I could make this comment now as opposed to later on.

It is unusual for me -- I usually talk off the cuff -- but I actually, because of the

import of this particular moment, I actually did write out my comments, because I wanted them to be said just the right way. They will take a couple of minutes, and that's why I wanted to start early.

As all of you know, this is for me a period of really quite significant change. Last month I left CDC after working at CDC for about 20 years, and that was a place that I profoundly loved, and it was very difficult to leave that position. And I am now currently relocating, as I think a number of you know, from Atlanta to Hawaii for a hardship assignment where I have begun a new position in the Department of Health and Human Services as the HHS representative to the Pacific Islands. This is a position that, at least for me, takes me kind of full circle, because I actually began my public health service career serving as a physician on one of those little tiny islands out in Micronesia.

Next week, another transition for me -- I'll actually be taking off the uniform and

retiring from the commissioned corps of the Public Health Service.

As would be the case with anybody, change of this magnitude is certainly disorienting. But I take a lot of heart from a quote that I ran across a few months ago. It says that to the fearful, change is threatening, because it means that many things could get worse; to the hopeful, change is encouraging, because it means that they may get better; but to the confident, change is inspiring, because it means the challenge exists to make things better.

To compound all of this change, this is my last meeting as a member of the AFEB and as the Board president. Even though I didn't really spend as many years on the AFEB as I did with the commissioned corps of the Public Health Service or with CDC, it does fill me with every bit as much melancholy and sadness as any of the other changes. I truly cherished my time on the Board. It’s been about a learning opportunity, a chance to interact with many wonderful and talented

people, and most importantly, to contribute in some small way to improve the health and well-being of the fine men and women of the Armed Services. It's been a absolute privilege to serve with all of you, both those who are currently on the Board as well as those whose terms have expired while I was president.

For those who weren't around at the time, I was kind of the accidental president to the Board. Mark LaForce, who was my predecessor as the Board president, unexpectedly took a position over at TEAS (phonetic), and as a result of that, had to resign as a member of the Board. He asked me about 2 weeks or 3 weeks before the meeting if I would mind chairing the upcoming meeting of the AFEB.

Unfortunately, that particular meeting, and some of you might remember, was scheduled to take place the week after September 11, 2001, and at the time Reagan National was still closed. All the flights around the country were really severely disrupted. I can recall having a lot of

discussions at that time with Health Affairs -- I think this preceded when you were actually at Health Affairs -- as to whether we should actually go forward with that particular meeting. We concluded that, as a show of solidarity with the Department, that we would carry on and actually hold the meeting, which was in Bethesda. I really was quite proud of the fact that we did that, and that so many of the Board members had the courage to come to that meeting in what were very difficult circumstances.

From my perspective, I would really like to think that that meeting started a period of renaissance for the Board, particularly a renewed sense of commitment to help the men and women in uniform during what has subsequently been a very difficult and challenging period. I hope that if there has been one thing that I have been able to accomplish, it's to establish a renewed sense of value for the work that the Board does as we have been able to work through a whole series of very difficult issues.

From my perspective, this really isn't my doing; it's your doing. I like a quote by Edith Wharton, who once said that there are two ways to spread light: One can either be the candle or the mirror that reflects the light. Without question, I really consider myself to be the latter. During my period with the Board, I've really been truly blessed to have the chance to work with three really wonderful executive secretaries -- those being Ben Diniega, Rick Riddle, and now Roger Gibson -- and to be really very highly supported by Health Affairs, particularly by Ms. Embrey, sitting to my right, and by Dr. Winkenwerder, and to be able to work with the really fabulous contingent of preventive medicine liaisons from all of the Services.

But from my perspective, the real key to the success has been the many fine members of the Board who over time have given so generously of their time and knowledge. So to all of you, I really want to express my admiration and gratitude, as you have made it very easy for me to

be the Board president.

Until I move into my new house in Hawaii, the last few weeks I have sort of been a vagabond, jumping from one BOQ to the next BOQ in Honolulu. I've stayed at Hickam, and I've stayed at Pearl Harbor, and now I'm out at the Marine base in Kaneohe. I also had an opportunity last week to meet with the PACOM command surgeon and have some extended discussions. The one thing that that has been able to do, it's allowed me to do what I enjoy most, which is interacting with, asking questions, and getting insights from the many fine airmen, sailors, soldiers and Marines out on the front lines. It has really reinforced my belief that they're the absolute cream of America.

As you all know, I've made one of the hallmarks of my time as the Board president the opportunity to visit as many military settings as we possibly could so that we had the opportunity to actually see things and interact with those who are on the front line. Even though many of you

had actually spent time in the military and have a fairly good understanding of the military, some of us haven't. Certainly those that have did so in the past, and things are considerably different in the Services than they were. Therefore, I really have considered it to be very important for us to properly to do our jobs as Board members, to really gain feedback from those who are impacted by our advice and recommendations, whether they're in boot camp or whether they run the bases. There's an old proverb that says, what you don't see with your eyes, don't invent with your mouth. I think that that's true. So it is really important for us to actually see things to better understand them, so we can provide the best advice to the Department and to the Armed Services. So I hope this particular tradition will continue, because it is really from my perspective a great reminder of why and for whom we ultimately serve.

Fortunately, I'm able to leave the Board in exceptionally capable hands, both with Roger as executive secretary and under the great leadership

of Greg Poland. I don't really have any advice for Greg, because he really doesn't need any. He is clearly every bit as devoted to the work of the Board and the military as I am. I think that there will be many great things from him as president.

I'll just end with one additional quote. This one is from Margaret Thatcher. She said, look at a day when you were extremely satisfied at the end. It's not a day when you lounged around doing nothing. It's one when you've had everything to do and you've actually done it.

I'd like to say I think that is the case with the Board, but I'm afraid it really isn't so. We truly accomplished a lot, particularly in the area of infectious diseases and keeping adenovirus on the front burner. But from my perspective, there really are many issues we've barely touched, including injuries, lifestyle behaviors like alcohol and tobacco, and the many sacrifices associated with the conflicts in Iraq and Afghanistan. I'm really hoping that there will be

opportunities to address these many topics under Greg's leadership. From my perspective, they are all major public health issues in the military, and I really believe that they should be addressed by the military's premier public health advisory Board. So I'm throwing that one out there as both a challenge and an opportunity.

So let me finish by again thanking each of you personally. The welcome mat is always out, should you want to come out to Hawaii and pay a visit. Absolutely, I'm truly honored to have had the opportunity to serve you in the Department, but most of all, the troops. So thanks very much.

(Applause)

DR. OSTROFF: As you know, I do like to crack the gavel. We have about 5 minutes before we get started. So for any of you who need to make a pit stop or make any phone calls or do anything else, please be back promptly at 1 o'clock.

(Recess)

DR. OSTROFF: My clock says 1 o'clock on

the nose, and we have a lot to cover, and so I'm going to go ahead and get started. An old friend of the Board is going to make some welcome comments -- welcoming comments, I should say. This is Colonel Eric Henchal, and thank you once again for hosting us.

COLONEL HENCHAL: Well, it's a great honor to have you here. I'm going to have to excuse myself; I'm still recovering from laryngitis. They told me I'm not infectious, but we'll let that one go.

It is a great honor to have the AFEB here again. You know, the AFEB and USAMRIID have this very long history. I don't know how many people know this. But it was actually an AFEB meeting in September of 1954 that first recommended and then endorsed the notion of doing ethically regulated clinical studies here at Fort Detrick to evaluate biological defense measures. And it was from that recommendation that the Army Medical Unit was established here at USAMRIID. It was actually the first unit to be dedicated

strictly to medical biological defense, and it really set the framework for conducting those studies, the clinical studies that were necessary at that time. And at that time, you have to remember that there were all these things that were emerging like the Nuremberg recommendations and others that had play in how that program was designed.

It was then, also, in 1969, and this is in January of 1969, that the AFEB recognized the stand-up of the new USAMRIID. Up until that point, we had just been an Army medical unit. Then in 1969, in January, the modern USAMRIID, the U.S. Army Medical Research Institute for Infectious Diseases, was established. This was prior to the decision by President Nixon in November of that same year to do away with the offensive program. So what remained there was then this Institute, that continues to be dedicated towards medical biological defense.

At this time, we are still faced with the problems of biological warfare. And we

recognize that we are also a nation at war. The operations in Iraq and the global war on terrorism are going to continue to challenge the use of our limited medical assets. So it is in that context that we continue to look at the AFEB for their recommendations in how we should employ the whole gamut of countermeasures in order to protect our Service members. That includes the vaccines and the therapeutics, as well as the medical diagnostics that are also the underpinnings of a good medical program.

So with that, I wish you a productive meeting and offer you also, then, also the services of my command group to assist you in any way during your stay here.

Thank you very much.

DR. OSTROFF: I'll take you at your word that you are no longer infectious. This is a plaque of appreciation for hosting us at the AFEB and one of the AFEB coins. The only other thing that I'll say is that we heard about this wonderful new $850 million building that you're

getting. So we hope at least your predecessors will continue to host us, because we are looking forward to it.

COLONEL HENCHAL: Thanks.

DR. OSTROFF: Next is Major Morningstar.

MAJOR MORNINGSTAR: Good afternoon, my name is Major Shannon Morningstar. I'm the deputy -- oh, I'm sorry, sir.

DR. OSTROFF: Hold on just a second. I neglected to let Colonel Gibson to make a couple of administrative comments before we launched into the program. So I'm going to turn it over to Roger. Thank you.

COLONEL GIBSON: I want to remind everybody that this is a transcripted meeting, and as such, when you speak, introduce yourself before you speak, and speak loudly so our transcriptor can pick up the information that we need. The meeting transcripts will be posted on the website in three weeks, about, right? Okay. When the transcriptor sends me the transcripts, we'll put them on the website. So the meeting slides will

be posted early next week on our website as well. Refreshments are available this afternoon out in the hallway, and tomorrow morning and tomorrow afternoon's sessions will also have refreshment. Restrooms are to the left -- once you go out this door, you turn to the left, and there are restrooms for the men and women down there. If you need a telephone or a fax or a copy, see Karen.

Finally, a couple of very small agenda changes. Colonel Berte is talking -- he is speaking today on Advanced Development Of Chem Biomedical Countermeasures for DOD on the agenda. That's a slightly different title than The Joint Vaccine Agency. And a major mistake on my part: The list of Board members on the front under tab 1 neglects Dr. Lednar, Dr. Oxman, Dr. Sherman, Dr. Ananth, and Dr. Ennis. This was an old list. I pulled the wrong one up and made copies of it and put it in here. My fault. I apologize. If you need background information on all of the Board members, go to www.ha.osd.mills/afeb. It's all up

there.

That's all I have.

DR. OSTROFF: Before we launch into the official meeting, I would be remiss if I neglect Ms. Embrey as the designated federal official. I think the reason I overlooked it is that Sal Cirone did such a wonderful job of making the statement this morning that I thought it wasn't necessary to do it again. But protocol requires.

DR. EMBREY: Well, what Sal said was good enough for me. But I do want to add my appreciation to Colonel Henchal for his willingness to host this meeting and for the outstanding support he and his staff provided, both for this visit here and over to ASNC as well. So anyway, without further ado, let's carry on.

DR. OSTROFF: Colonel Gibson has one more brief announcement.

COLONEL GIBSON: Tonight, dinner is at Dutch's Daughter. We'll be leaving at 7:15 from the hotel lobby to get there at 7:30. Raise your hands or see Karen or Sue over here. Make sure we

know how many folks are coming. We need to call Dutch's Daughter and tell them how many people are coming. We need to get that done, get a count. That's it.

DR. OSTROFF: Great. Now, without further ado, one of the requirements that the Board has is our annual ethics training. Here, helping to do this, is Major Shannon Mao Morningstar, who's the ethics counselor and deputy staff judge advocate at Fort Detrick. Thanks for being here. Her slides are in tab number 3.

MAJOR MORNINGSTAR: To give you kind of a heads-up here, usually this training I've done, I've done it for about a year now. It is usually to all Army personnel, and you are going to see the requirements for that. You are going to probably sit here and think, well, maybe I'm from a different service, or I'm civilian personnel; how does this apply to me? I think that if you see that these rules apply to Army personnel, if you work with Army personnel, they do help you in your interaction with us. Also, you're going to

see an ongoing trend in here. You're going to see the reason that the ethics arena has become more and more under the microscope, so to speak. That has happened due to a series of activities that happened over the last year, and I'll talk about this a little bit as we go along with this briefing.

Now, usually when I do this briefing, I tell people, the Army is always interested in the bottom line up front. So I've done that. The most important slide that you'll be seeing is this slide, which has my name and my phone number on there. You're going to see that this is going to be so much information compressed into a short amount of time, it's going to be very hard for you to utilize this information as your own, based just on this one-hour training. However, all I'm trying to do is give you some idea of what the issues are. Therefore, if you run across it, you can e-mail me or call me, and I will either answer your question or certainly get you to other folks who can.

DR. OSTROFF: Can you give us your e-mail, please?

MAJOR MORNINGSTAR: Sure. It's shannon.morningstar@amedd.army.mil.

Okay. First of all, there will be some of you out there who have had some of this ethics training before, and for others, they may say, I've never had this training before, and there is a good reason for it. Prior to this, this was not an annual requirement, okay? On 9 April of 2004, our then-acting secretary of the Army, Mr. Brownlee, he changed the standard. Previously, it used to be that only folks that had to file what we called a SF350, which is a confidential financial disclosure form, were required to receive this one-hour training. The training could be done by computer, or there were other ways of doing it by -- sending the PowerPoint to someone else.

Now, what Mr. Brownlee did was to change all of that. He said, what I want now is for everyone in the Army to receive ethics training,

and I want the ethics training to be face to face. As you can see, it is a significant change. I think as I go onward, you'll see why this change occurred.

Okay, I've been an ethics counselor now -- this is the fourth time. When I first came into the Army in 1992, the Army had an Army regulation that controlled our ethical guidance. The Army ethical regulation wasn't too bad. It was not more than 50 pages, and you could read in one sitting if you wanted to.

The year after I came in, we adopted what we call the joint ethics regulation, and that is a single source guidance for all ethical guidance across all of DOD. It went from being about 50 pages to being about the length of a phone book. It is quite extensive.

During that time, you know, I had more and more people ask me different questions about why it's important to act ethically. I basically came up with three different reasons. First of all, on a personal level, we all want to do the

right thing. Now, second of all, there is a pragmatic reason. If you look at all the studies out there, it shows that any organization, any corporation, and indeed, any country that is corrupt is more efficient. So in a macro sense, we are actually better serving ourselves if we live an a less corrupt society. Of course, finally, there is a legal basis, okay, and I'll talk about a legal basis in just a second.

Now, let's talk about what the Army did. In essence, I talked to you about this very large phone book out there. What the Army did was, the Army was very nice and compressed all that information into this 14 principles of ethical conduct. Okay? So any time you see one of these boxes, that's one of the 14 principles. They try not to hit you too much with one thing at a time.

Now, if you look at the general principle, this what guides the Army, but certainly you see it's a federal guidance that applies to all the Air Force and naval folks also, that the public service is a public trust and you

must -- your loyalty to your duty must be above any personal gain. Remember, I talked about the legal basis? If you look at the Army and officers in the military, when they came in, they talked about, this is the oath they took. Part of that oath says, "I will well and faithfully discharge the duty of your office." This is a legal basis by which we require them to act ethically.

This is a point at which I give some examples of people who did not act ethically. Really, if you think about this, this is kind of like someone throwing a stone into the water, and what happens is, there is a very wide-reaching instance of the result of their activities. The first individual you're going to see there, it's going to be on my right here, it is an individual -- he was an administrator for an Indiana school system. He was given about a million dollar budget to update these computers in secondary schools. Instead of doing that, he basically formed what we call a nonprofit organization which he was the sole member, and he

began writing out checks to himself. He in fact embezzled over $300,000 before they were able to catch on to what he was doing. Of course, the computers were never updated.

The lady you see in the middle there, if you all live in the Beltway and read the Washington Post, her picture may look somewhat familiar to you. She was the president of the Washington teachers' union. She and about three or four of her co-conspirators embezzled about, they think, anywhere between two to five million dollars from the teachers' fund. What that did was -- and in fact, she was off purchasing things such as fur and jewelry and designer clothing. One thing that she did not do was pay the health insurance premium. Many retired teachers in the Washington district, their only source of health insurance was through the group insurance they got from the union. In fact, she caused many of the people during a very critical time in their life to be without health insurance.

That lady you there with the glasses on

looking at the computer, she's probably the reason why there is so much interest in ethics right now. Here name was Darlene Druyan. She was the number two acquisition officer for the Air Force. In fact, what happened was, over time it was discovered she had given quite a controversial contract over to this company, Boeing. In fact, there was some issues with it. When Congress started looking into it, they realized what she did was, she had entered into a post-government employment contract with Boeing while she was still on active duty. That in itself was not impermissible. However, she did not disqualify herself from acting with anything that had to do with Boeing. So in fact, she was on one hand saying to Boeing, I'm going to come work for you; on the other hand, she was deciding on a contract in which Boeing was one of the competitors. In fact, she did award one of the contracts to Boeing and quietly retired and therefore, just a couple of months later, popped up as one of the VPs of Boeing. This eventually was all brought to light,

and she was fired and the VP of Boeing was fired. In fact, both of them have appeared before federal court, and she has been sentenced to prison for about 9 months. But that is the only merest beginning of what happened to that. Thereafter, there were so many negative consequences that resulted from that. First of all, certainly the contract -- one of the most negative consequences was, Boeing, in reliance with that contract, had in fact started up a factory that was up in Seattle. They hired a bunch of people. What happened at this point was, Congress went back and said, look, this contract, we can't go forward with it. It has to be redone. So what happened was, much later all these folks over in another state ended up losing their job because this contract could not be carried out. So you're going to see, there is a wide latitude of things that may happen if ethical activities are not followed.

One of the great issues that you're going to see is concerning conflict of interest.

We talked about the 14 principles. I'm going to say, in one form or the other, many of these 14 principles have to do with conflict of interest. The main thing is this: Federal employees may not take official actions in matters in which they have a personal interest.

Let's talk about, there are certain people whose interest is so closely aligned to those of you that they are considered you for the purpose of those conflict of interest laws. Who are these people? These people are your spouse, your minor children, people you're in business with, and also, as in the case of Ms. Druyan, people you are negotiating with for postgovernment employment.

Now, I often have people in the Army come and ask me -- they say, hey, I'm thinking about coming out and working on the civilian side. I've sent out a resume. Does that mean I've undertaken the financial interest of every company that I've sent a resume to? That is not what it means. If you look at the joint ethics regulation

the guidance is "negotiation, however slight." Really, negotiation really attaches from the time the company comes back to you and says, look, I'm interested in you, let's start talking. I think that at that point when the negotiation begins -- and certainly, if you're negotiating with a company whose work has impact on your official duties -- you have to disqualify yourself. You can't do both.

One of the things I usually tell people who come to me for ethical items is this. You have to think of your life as a train. Your train runs on two tracks. One is the track of your official duty. One is the track of your personal life. All is well if they ran side by side, yet never touching. Once they get to the point where they touch each other, such as postgovernment employment, you could get into a great deal of trouble.

The next bullet I want to talk about is the actual versus appearance of conflict of interest. Now, I think it is very easy to look at

what is considered actual conflict of interest. You just look at what your duties are, and then you look at what your personal life is. Now, the appearance of conflict of interest is something that is a little trickier. It's trickier because it includes what I consider an X factor. Now, the X factor means it’s really in the eye of the beholder, okay? And what that means, as you get more senior in your position, more folks are going to be looking at your official life. And therefore, things have previously may not be an actual conflict of interest may to outsiders look to have an appearance of conflict of interest. It is something that is inevitable as people go further up in their rank and further up in their prominence. You just have to be very careful with that. And the joint ethics regulation -- also an ethics counselor -- will be able to steer you in and out of there.

Finally, I want to talk about the last bullet: Disqualifications and other remedies. There are many, many remedies that can be done.

The main thing is what we call disqualification. What you're saying is, you go to the boss and you say, look, I have something happening in my personal life. For example, I'm negotiating for postgovernment employment or I'm moonlighting. Therefore, I cannot act in my official duty with respect to certain companies. And you write a disqualification letter and you notify your boss. You make sure that someone else is given that piece of the duty. You just can't have two things overlap.

Let's talk about insider information. Really, you see the information there. The guidance in the 5 CFR says, "Information gained through federal employment that the employee knows or should know is unavailable publicly may not be used for financial transaction or for personal gain."

Now, many people will say, what exactly is nonpublic information? And certainly this is not a complete list. But anything that is covered by the Procurement Integrity Act, any classified

information, any information covered by the Privacy Act or the Trade Secret Act, all of that is nonpublic information.

The other point I want to make here is this. Inside of these -- the Procurement Integrity Act or, say, the Privacy Act -- there is a provision in there prohibiting you from making this public without the proper legal authority. So therefore, if you use nonpublic information, not only will you violate the joint ethics regulation; you probably will have violated another federal guidance, and violation of two federal laws is never a good idea.

Now, the issue of gifts, this comes up quite a bit. You're going to see a very, very long explanation here. I'm going to ask you to take a quick look at it, but I'm going to try and make it less confusing for you. This is indeed one of the most confusing areas, because the rules are different. They're different when you're dealing with different people.

Now, the first law, the Standard of

Conduct office of the DA, they always want us to push this. They say, look, there is no rule saying you have to take a gift. You can always refuse it. Ethically, it is always okay to refuse. Okay? So if you want to skip any kind of legal analysis, you can always say no and that's never going to be a problem.

Now, when we look at the gift rule, I will say, the first time I read the gift rule, my first inclination was to say, wow, this must have been written by an attorney, because as you can see, all attorneys do the same thing. You start out with a bright-line rule, and you start thinking, okay, this is an easy rule to understand and remember. I'll have no problem. But as with all things written by attorneys once you have the bright-line rule, there are exceptions, exceptions, and exceptions, okay? That's what happens with the gift rule.

Here's the gift rule. You start out with the guidance. The bright-line rule is, a gift is any item of monetary value. However, you

we're going to immediately start with the exceptions. The first exception is what we call a nongift exception. The second is called a gift exception. The third is a completely different one; it talks about the source of where the gifts come from. Let me first go to the first gift exception. That's another way of looking at it. The general rule, any item of nonmonetary value, and the three different exceptions.

Now, I began by saying, a gift is any items of monetary value. However, immediately we start out with -- there are things that are considered nongifts. It's an items of such limited value that in essence they are not really considered gifts, okay? So right off the bat, the definition is items of little intrinsic value intended solely for presentation. That's a very long way to say a plaque. A plaque is usually considered a nongift. Coffee and doughnuts are considered a nongift. And certain discounts and offers made to a group -- and this is something you see, like sometimes if you stop at certain

fast food stores, especially me being in the military, they give you like a 10 percent off, 10 percent off on my hamburger. It is considered of such minimal value, it's considered a nongift.

Now, we're now in the second class of gifts. These are gifts considered -- they are going to have a little bit more value, but there is an exception for them. Let's talk about the first rule -- very confusing. It talks about a value of less or equal to $20, but not more than $50 per source per calendar year.

Well, when I say this, most people say, I hear this rule, but what does it really mean? Let me give you an example. Let's say you are -- for example, let's say you are a doctor, and you receive a promotional item from a pharmaceutical company that you deal with. This item is less than $20. Can you accept it? Yes. They send you another item the same year. Can you accept it? If it's under $20, yes, you can. Now, if they send you a third item worth less than or equal $20 in the same year, now you can't accept it,

because, you now went from 20, 20, 20 -- now you would hit above the $50 ceiling. So the item itself has to be less than or equal to $20, and not more than $50 from any source during a calendar year.

Now, I have people ask me things like, well, what if the doctor receives two promotional items -- one is $15 and one is $30. Can you accept both, because together, they are not more than $50? And the answer is, you can accept the $15, but not the $30. It has to hit both the rules.

Now, we talked about a gift to a class or group of employers or soldiers that are able to be excepted. Now, the best examples to think about this is something like, sometimes places like Disney World, they have military weekends, and your military members and their dependents can go, let's say for example, half price. Okay? That's not a de minimis thing, because a ticket to Disney World is quite expensive. However, the gift is to a group or a class. A group or a class

is all military members. It is considered such a large group, it is not given to you specifically. So that is also a gift exception which you may accept.

Now, this one may be kind of near and dear to your hearts: Awards and service achievements. I have had researchers come to me and say, I went to this one thing and when I came back, I was given a plaque, and with that plaque, I was also given a check for X number of dollars, and the question is, can I accept this service achievement award? And unfortunately, my answer to them is always I have to check, because it is something that is unknowable until I see the actual item. What happens, I can tell you, is the joint ethics regulation has certain guidance, and it says, if you are in a program and this program meets these certain criteria, then yes, you may accept. So usually what happens is, folks come to me and they show me what it is and what program it is, and I actually go on the internet and I do further research to verify what they are saying.

Then I provide them with a legal opinion saying whether or not they can accept this. And most of the time, people who deal with the military understand this provision and they do tailor their program in such a way that people can accept it. But in any case, I do want to stress, acceptance is really not authorized until your ethics counselor has rendered you an opinion. Also, if it's over some dollar amount, you will have to report this in your financial disclosure.

Now, the last part is permitted by statute. I want to talk about gifts from foreign governments. Especially senior commanders have an opportunity to travel outside the country. They often may receive gifts from foreign governments. And usually the guidance is, you may accept the gift if it's under a certain dollar amount. And the last time I had to check this, it was $285. However, I always recommend individuals who receive gifts from foreign governments to still check with the ethics counselor, simply because usually gifts from a foreign government, it's very

difficult to ascertain what the fair market value is. They usually give you an item and you're looking at it and it is a jeweled sabre that you say, I don't know what the fair market value is. But certainly we have historical data, and I can always call the State Department to determine what the fair market value of the gift is.

Now we've gone through the first three exceptions with the last exception that is available for the military folks. You're looking at gifts outside the government and gifts between federal employees. Now, I'll talk about these step by step. Why is a gift being offered? Who or what is a prohibited source? Is acceptance of any offer from a prohibited source improper, and if it is improper, what do I do now?

Now, the big exception here is, why is a gift being offered? Is it being offered because of your official position or because of your personnel capacity? Now, if it's being offered because of your official position, then all the gift rules apply. However, if it is offered

because of your personal capacity, then the gift rules do not apply and you may accept. You may say to yourself, how do I know why they're giving me this gift? Well, there is a easy rule of thumb you can use, okay? Take a look at the gift and ask yourself if right at this moment, if I am unemployed, am I still be going to be getting this gift? If the answer is yes, most likely it is being given because of your personal capacity. For example, you are a military commander. Your wife, the government contractor, gives you an anniversary gift, okay. You can say to yourself, if I'm unemployed, would I still be getting an anniversary gift? You could usually answer, yes I will, but the gift won't be as nice. In any case, it is given because of your personal capacity and you may accept.

Now, let's talk about the official position, though. Now, I know the universe is wide and all things are possible. But in general, if a gift is not offered due to your personal capacity, then it is most likely given because of

your official position. And therefore, most likely it is from a prohibited source. So the next question is, can you accept any gift from a prohibited source? Here is the basic guidance. "An employee shall not solicit or accept directly or indirectly a gift from a prohibited source or given because of the official position." However, remember the gift exception we talked about before still applies. So if the prohibited source gives you a plaque, you can still accept, because it is a nongift. Now, you may be asking yourself, what exactly is a prohibited source? The net is cast very wide. If you look at the guidance, it is anybody who does business with the Army or whatever your branch is, seeks to do business with the Army, conducts activities that the Army regulates, or whose interest may be substantially affected by the Army. Now, if you look at these four and you say to yourself, that's quite a lot to remember, I think the only thing you have to do is to remember the last bullet. If you look at it, all the three bullets above may be subsumed

into the last bullet. So anyone whose interest may be substantially affected by the Army may be a prohibited source. Now, if you have any question about whether someone who provided you a gift is a prohibited source, that is a perfectly legitimate question to ask the ethics counselor. Usually the ethics counselor will sit down and talk to you about your job, talk about the people who are offering you the gift, and you can come to an understanding of whether or not it is a prohibited source.

Now, I want to give you some examples of prohibited source. For example, we all know that defense contractors are prohibited sources. But people are often surprised. Professional organizations, nonprofit organizations, even educational institutes may be a prohibited source. You all sitting out there may be saying, how can an educational institute be a prohibited source? I'll give you a great example. Here at Fort Detrick we have a lot of congressionally mandated resources. That means Congress gives us the

money, and we basically give grants out to different research institutes and educational institutes, and we let them do research with that. Well, now, the grant process is also a competitive process. Therefore, in relation to us, many educational institutes are prohibited sources, because, yes, in fact whose interest may be substantially impacted by the Army.

I wanted to go over this very quickly. This is an issue that is coming to the floor more and more now, okay? The military has a tendency -- we're outsourcing a lot now. We have a lot of contracted personnel. They're running along right outside on the battlefield. They're right next to us, they're doing a lot of things, great things for us. However, contractor employees are a prohibited source. They are not the same as DA employees. The thing to remember is, no matter how well you like the contracting personnel and how well they work with you, their final relationship with DOD in particular is a contract, and eventually that contract will be up

for renewal or it might be revoked. You don't want DOD itself to be open to criticisms that you are renewing a contract, because the contracting employees are giving you presents. So you have to have somewhat of an arms-length transaction on the ethical side.

What can be done if a gift is offered? Well, certainly if a gift is offered, remember, our first rule is, you can always decline. Now, the second thing is, you can receive the gift as a gift to the agency. For example, many times our general will go traveling outside. What you see is, many general officers will go traveling, they go to a foreign country, they receive a gift. They don't have to accept that gift personally. They can actually accept the gift on behalf of, for example, MRMC, and it's placed on the property book of MRMC. So when that general officer retires, the gift stays there. In that sense, the gift is not counted as a gift personally. Consumable gifts are usually okay, especially if you share them with your officemate. You can also

pay market value to the donor. Now, if you pay market value to the donor for a gift, it is no longer a gift; you just bought yourself a new item.

Finally, sometimes gifts are done through a presentation format. It is very difficult when it's in the middle of a presentation to say, stop, I can't accept the gift. You can certainly accept it for a duration, and you come back and write a polite letter and return the gift. Certainly there are examples of that. And if you have some question about how not to offend people, I have many samples of that.

Believe it or not, that is all one big thing, gifts from outside sources. Now we're going to talk about gifts between government employees. Once again, it's a lawyer type thing. You have the great general bright-line rules, and then we're going to have some exceptions. The bright-line rule is this. If somebody works for you and makes less money than you, you can't accept any gifts from them. On the other side of

the house, if you work for your supervisor or someone who makes more money than you, you can't give them a gift. That's a general rule, and there are some exceptions. For example, you have what we call the de minimis exception -- once again, of such minimal value. I don't know how many of you have these office Christmas gift exchanges, but they always keep it down to about $10. That's where this comes from. If you have a $10 per occasion between federal employees, that is considered okay. It is a de minimis exception. Birthday gifts, vacation souvenirs -- once again, no cash.

The last bullet there, hospitality at an employees home. Feel free to invite your supervisors over to dinner. There is an exception for that.

Now, the one we see most often is the special infrequent occasion. For most military personnel, it is when the supervisor is either retiring or about to go off to a new job. Now, I will say, there is a whole series of rules that

talks about when you can go ahead and solicit the gift. Now, I'm going to take a minute to go over the solicitation rules. I know many of you are not in the Army and also have a lot of civilian counterparts out there. But I do want to show you in the Army, there are just so many regulations. They are very, very careful with this. You don't want this to get out of hand. For example, if you're soliciting gifts for a supervisor who is about to retire, the solicitation has to be done by the most junior person in the office. Junior, so no one feels no pressure to give. If you have a list, a list of who contributed, you may only keep a list to say, here are the people I have already solicited from. This is to ensure don't solicit the same people over and over again. However, you may not keep a list of, "This is Bob Smith and he gave $10." There can be no dollar association. A very existence of that list can be considered coercive.

Now, the JR says, you may solicit no more than $10 for any kind of attention for this.

Now, an individual may decide they want to donate $15 or $20. That's okay. But the person who is soliciting may not ask for more than $10. Finally, the value of the gift may not exceed $300 per donating group. So if you have people coming around and they want to give the supervisor a gift. It's up to you how you set up your group, how many people are in that group, but no matter what, the gift itself should not go beyond $300. There is an exception, okay? I will say that. However, usually the exception is run through the ethics counselor if you want to go above $300. Most places I've been to, the supervisor who is leaving themselves give guidance and say, I don't want any gifts beyond $300 per donating group.

Now, number five, "an employee shall put forth an honest effort in the performance of a duty," and he says, I did nothing all day and still got paid for it. Probably not a good idea, okay? Now, I don't know how many contractors we have out there, maybe none, but certainly, anyone, you do not want to be making unauthorized

commitments or promises of any kind on behalf of the government, because in the end, if you don't have the authority to enter into these contracting agreements, you may be held personally liable.

Now, this another iteration of a conflict of interest. Do you see that? "Employees shall not use public office for private gain. You shall act impartially and not give preference or treatment to any private organization or individual." Now, where you see that, the private organizations, there are may things I want to caution you about. Especially military personnel and DA civilians -- we do not manage private organizations in our official capacity. Okay? We can be a liaison. We don't officially endorse. We don't support fundraising or membership groups. There are specific exceptions within the joint ethics regulation, but one of them is the combined federal campaign. There are also certain support that we give to private organizations that are in statute that allows us to do it. For example, the Boy Scout

Jamboree, there is actually a federal statue that allows that. But in general, private organizations, we do not have unauthorized relationships with them. There are many times when we look at private organizations we think, they are doing a great thing for us. And it could be. However, the guidance of how we interact with private organizations are set forth in the joint regulations, and I'm sure in the perspective regulations. I know that in the Army, they have quite an extensive regulation about that also.

Logistical support of private organizations is usually run through Army regulations.

Now, "employees shall protect and reserve federal property and shall not use it other than authorized activities." I am just going to go over this very quickly, because it does not apply to all of you. But the main thing is this. The use of government property, the main concern here is the use of communication systems. Computers, telephones, e-mails, internet. Okay?

There is official use and there is authorized use. And official use is actually what it sounds like. It is what you need to do your official duties. Now, many people have questions, what is authorized use? If you look at authorized use, the best way to define it is, minimal personal use that is authorized by your supervisor. And it has to fit these five criteria. So it doesn't adversely affect official duty, is of a reasonable duration or frequency, serves the legitimate interest -- now, many people stop me right here and say, how can my minimal personal use serve a legitimate public interest? I will give you an example. You're sitting at your desk and your spouse calls you up and says, I think I might have bounced a check. You can, A, say, okay, I'm going to get on the internet right now and move some funds around and then it will be covered. Or you can jump up and say to your boss, I need to go to the bank and I'll be back in an hour and a half. In those types of circumstances, the military basically says, look, it serves all the legitimate

interest to let you use it for five minutes. It doesn't adversely reflect on DOD. I think we all understand what that means, really. You should not be using your DOD computer for any gambling, no downloading of pornography, and does not overburden the system. I will say that that last bullet, "does not overburden the system," and is coming into play more and more often now.

There is only really thing I really want to get across here, which is cell phones. It used to be in the Army -- there's a change -- it used to be cell phones, official cell phones, only could be used for official business. Okay? Now, Army cell phones can be used for official business and authorized use. That's what they added, authorized use. So it can be used for minimal personal use, but only under very limited circumstances, usually when you're traveling and usually only to tell your family where you are and any change of scheduling. When you are not traveling, there are even more limitations. I think the only point I would say here is this. If

you're not traveling and you have a government cell phone, can you make a long distance call on the cell phone? The answer is yes. However, if you look at the bulletin here, you can make this long distance call, but the Army doesn't want to pay for it. You can make a long distance call if you can charge the call elsewhere.

Use of subordinates. Subordinates are really considered a part of Army resources, and you should not use them to run your personal errands, meals, shopping, dry cleaning or whatever. I have a picture of ex-Secretary of Health and Human Services, Ms. Donna Shalala when she was the secretary of Health and Human Services. There was actually a picture of her in the Washington Post when she was standing patiently in line buying her own stamps. This is good, and I think one of the points there was to show, even though she was a high ranking official, she was not above running her personal errands and was not about to use her subordinates to run her errands.

We're now going into the catch-all provisions. And the catch-all provisions, we're going to see the conflict of interest come up again. Employees are prohibited in engaging outside employment activities include seeking or negotiating for employment that conflicts with your official government duty. You are obligated to disclose fraud, waste, and abuse. Certainly the IG would be a great place to start. You must satisfy in good faith your obligation as citizens -- that means pay your parking ticket, pay your taxes, all these things we are required to do. Employees are required to adhere to all laws and regulation that provides equal opportunity, and you shall endeavor even the appearance that you are violating the law.

Now that we get to the 14th principle, that is the end of my presentation. I am certainly available for any questions or anybody who wants to e-mail or call me later. I can chat with them about any of this stuff.

Thank you very much.

DR. OSTROFF: Thank you very much for that overview. I know it is difficult to do this every year, but it is very important we have this type of grounding. We need to ask if there are any questions or comments from the Board members.

(No response)

I'll take that as a sign that your presentation was absolutely crystal clear. Thanks very much.

Our next presentation is a subject that is near and dear to the Board. For those members of the Board who are relatively new, this is a topic and an item that we have been dealing with for an extended period of time. And if I consider one issue the signature of my term as Board president, it's probably this one. So we appreciate the opportunity, at least I appreciate the opportunity to get one more update on the status of the reacquisition of adenovirus vaccine, and we have Dr. Lawrence Lightner, who's the project manager of pharmaceutical systems at the U.S. Army Medical Research and Materiel Command.

And I appreciate your willingness to be here.

MR. LIGHTNER : Thank you. I'm presenting this update on adenovirus restoration on behalf of Mr. Bill Howell, who is the MRMC deputy for acquisition. And I'll be following this basic outline in my presentation. I'll give you a little bit of a broad status of where the program is, and then I'll go into each of these bullets in a little bit more detail.

I think we're all familiar with the basic objective here, and that is to produce a safe, efficacious FDA-licensed vaccine to product US military trainees from adenovirus types 4 and 7. Dr. Winkenwerder has officially established a requirement for adenovirus vaccine. Now, this is an important document for us, because until he signed this letter, there was not an official -- in the eyes of the Department of Defense -- requirement for this particular vaccine. This document gives us our credible requirement that's recognized across the Department of Defense, and it will carry us to the actual production phase of

the vaccine.

Now, we will still need to have a capabilities production document for this vaccine at the transition to production and procurement. But this gives us the time that we need to draft that document and staffing -- staffing time nowadays for a requirements document takes up to 12 months, 12 to 18 months. So this gives us the time that we need to do that.

This is the timeline that was presented at the September meeting of this group, and this is the current timeline. To save you the time of trying to sort through the small print, the only real change in the two charts is that there is a 2-week delay in this plan that was due to a delay in processing samples from the phase one study that I'll talk about in a minute. Now, the goal of having an approved vaccine by the end of 2007 has not changed. Obviously, reaching that goal is going to be contingent on everything falling into place exactly as planned, which we know the likelihood of that happening is -- well, it's not

100 percent, let's put it that way. We know there are risks. I'll talk about some of these risks a little bit later on and what we're doing to minimize those risks.

Now, this plan will be revalidated and re-baselined by the new milestone division authority soon after he or she arrives at Medical Research and Materiel Command. That will be General Martinez-Lopez's replacement.

This is a summary of the status of the funding requirements for the vaccine restoration program. We received additional FY04 and FY05 funding to cover the cost increase in the program that was due to a scope change in the redevelopment and some indirect costs on the contract. We have a funding program to support the current contract costs estimate from FY05 out to FY07. But there's one cautionary note here: The contract is a cost plus fixed fee contract, so there is always potential for cost growth in that type of contract. Additionally, program funds are required for the procurement, the initial

procurement of the vaccine and vaccine sustainment in the out years. And in that vein, we have already initiated the dialogue with the Defense Supply Center in Philadelphia. The product manager has gone up there and met with managers to discuss the follow-on procurement of the vaccine. We're in the process of coming up with a cost estimate for that, and we will 'll continue working this dialogue with the Defense Supply Center up in Philadelphia so we don't run into the same situation that we ran into with the old vaccine.

The clinical development status. Currently we are finishing up the phase one study. These are the objectives of the phase one study. The primary objective was, this was the first in-human safety study of the material, the new vaccine material that was produced by Duramed at the Virginia production facility. And then you see there a couple of secondary objectives of the study.

This is just to refresh your memory of

the design of the study and for the new members to give you an idea of the design of the study. The study was executed at Fort Sam Houston, Texas, in military personnel in advanced individual training, 91-Whiskeys. It was executed jointly by a medical staff, by physicians from the Walter Reed Army Institute of Research and personnel from the sponsor, Duramed.

This is a summary of the recruitment and enrollment in the study. Four hundred and twelve volunteers were screened. Volunteers were enrolled if they were seronegative for adenovirus type 4 or 7 or both when they were screened. We had 58 volunteers that were actually vaccinated and 54 volunteers that completed the study. The 180-day follow-up will be completed at the end of this week.

Now, the data from the trial are still blinded, so we don't have specific results to give you at this time. We'll be able to discuss those results at the next update for the Board. However, there are some observations that are

listed on this slide that were made during the study. The vaccine was very well tolerated. Seroconversion was approved. Virus shedding was observed, and there were no training days lost to side effects from the vaccine.

Now, I'd like to shift a little bit into the manufacturing of the vaccine. I think most of you are familiar with how this vaccine is constructed. It's actually a pill that's given with an inner virus core and a polymer coating around the core, an enteric coating. Now, in producing this pill, there is only a very slight margin of error to ensure that the coating is the correct thickness. If the coating is too thick or too thin, the vaccine is ineffective. So this puts a premium on manufacturing procedures, and it has presented a challenge for the contractor. And Barr has pointed out many times that if they had just taken the specifications they got from Wyeth and tried to reproduce this vaccine, it wouldn't have worked. So there is a continual tinkering with the manufacturing to make sure that the

vaccine is precise.

Here's the current status of the vaccine manufacturing. I'd like to touch a little bit on the third sub-bullet. The manufacturer has had some problems in the growth of the WI38 cell line that is currently used to propagate the vaccine -- or the virus, rather. As a result they're looking at the possibility of switching to an MRC-5 cell line, which is a little bit younger cell line and seems to be a little bit more healthy. Now, this is currently still under discussion. We are still discussing it between us and the contractor. And it will further be discussed with the Food and Drug Administration to try to nail down what some of the ramifications of this will be. Obviously there is some potential, if you switch the cell lines at this point, that you're either going to have an impact on either the schedule or the cost or both of trying to produce this vaccine. Now, the trade off will be that there is a potential to have a little more secure reproducible production process and a more viable vaccine. Again, we'll

have an update on this at the next AFEB meeting.

In terms of regulatory status, the sponsor requested a meeting with the Food and Drug Administration. The FDA responded that they thought the meeting was a little bit premature, in that we don't have the unblinded results from the phase one study yet. So they agreed to meet soon after the unblinding of the phase one study, which is scheduled for the first week in April at this time.

At that meeting, we'll discuss the data from the phase one trial. We'll talk about where to go next in terms of a precise clinical plan. And we'll also talk about the CMC issues, including the potential switch of the cell lines.

Now, the next clinical study, as I just mentioned, kind of depends a little bit on the meeting with the FDA in terms of the exact size of the study and the exact parameters that will be looked at in the study. But it will most likely be done in one or more military training sites. So we've already began consultations with these

training sites. Again, Dr. Winkenwerder was very kind and sent a letter out to all Services requesting their assistance and the use of basic training installations and support for clinical studies that would occur. TRADOC has agreed to support testing at Fort Jackson and Fort Leonard Wood, and the Navy will support testing at Great Lakes Naval Training Center. An initial visit has been made to Fort Jackson back in the first week of March, and a team is going out to Great Lakes tomorrow, actually, to talk to the people out there.

The execution of the current clinical plan is, again, dependent on the outcome of the phase one study and the meeting with the FDA, the manufacturing and availability of vaccine, and then the integration with the services training schedule. Again, we have to be very sensitive about going into these training sites and the potential for causing interference with the training schedule. So it has to be tightly wound.

This is a short term plan for the next 3

months. I won't go into each of these bullets, but you can see that it's an ambitious plan to look at various parts of the program. And this is a little bit longer range plan over the next 6 to 9 months. We need to produce additional vaccine for the trial. We need to solidify the plan for the next clinical trial. And we need to requalify the manufacturing facility. What's not on this slide, and I've already mentioned it previously, is that at some time during this time frame we'll hold a milestone review for the new milestone decision authority to reevaluate and re-baseline the program from an acquisition standpoint.

Finally, these are some of the potential risks that we perceive in the program. Any or all of them, again, could impact the baseline performance or cost parameters that we've set. We're trying to manage these very aggressively through weekly and sometimes two or three times a week meetings between the product management team and the contractor team to address any issues as they come up.

Now, the product manager for the adenovirus vaccine, Captain Eric Midboe, the project manager from Duramed, Dr. Alan Liss, and the technical lead from the Medical Research and Materiel Command, Colonel Wellington Sun, are all in the room here, and they will help me address any specific questions that you might have at this point.

DR. OSTROFF: Thank you very much for that presentation. I am really pleased to see the continued progress and the steady forward movement in terms of getting us to the ultimate goal of getting this vaccine reestablished as quickly as possible. I might ask the representatives that are here that you just mentioned if you have any comments that they would like to make from their perspective before I open it up to the Board members.

Yes, and please identify yourself as well. And you have to come to a microphone, because this is all being recorded now.

DR. LISS: Hi, I'm Alan Liss, project

director from Duramed Research, the proprietary arm of Barr Laboratories. First of all, I want to thank Dr. Lightner and his group for the participation and, of course, helping us. And I also thank and give a fond farewell to Dr. Ostroff for his retirement here and leaving the Board, at least.

And I'd say one important thing is that it ain't over yet. We encourage you to please have as much support in the future as we have in the past. There are a lot of moving parts to this, and we all know that we have the same goal in getting an effective vaccine back to the troops in a fast and economic time. So we're going to need all your support, and I invite all of you, again, if you ever want to visit our tableting facility in Virginia and to offline, officially or unofficially, to add any comments or ask questions, we're always open for your expertise. So thank you very much.

DR. OSTROFF: Thank you, Dr. Liss.

I have one or two comments before I open

it up to questions. One of them is, I'm a little perplexed by this issue of integrating the trial with the basic training schedule, because at least from my perspective, the disease is far more disruptive to the training schedule than the clinical trial ever will be. And so it disturbs me a little bit that that would be a major issue with some of the basic training sites.

Can you give us a little bit of an idea of what was done to encourage -- I do appreciate the letter that Dr. Winkenwerder sent out -- to encourage as many of the basic training sites to participate as possible? And what are the implications in terms of keeping on schedule to having a limited number of sites, as opposed to having a wider array of available sites to be able to do this? I must confess I'm a little chagrined not to see the participation of the Air Force, as one example.

UNIDENTIFIED SPEAKER: I think I'll let Colonel -- this is more in Colonel Sun's area. He's been working it pretty hard.

COLONEL SUN: To answer that question, first of all, I'm Wellington Sun. I head the Department of Virus Diseases at Walter Reed Army Institute of Research, and right now the clinical and technical lead in this adenovaccine project.

I agree that the translating the requirements all the way from the Secretary of Defense of Health Affairs all the way down to the level of drill instructors is a challenge. I think that even though we all in this room realize the need for this vaccine, to make that clear to the drill sergeant and to the local commanders, whose main mission is to make sure his troops graduate on time with as little attrition as possible, I think is a challenge before us. And doing the phase one study, we encountered some of that. And it is really critical that we go to these sites and make all the connections, cross all the T's and dot all the I's as far as the chain of command.

And so while I understand the direction that we need to go, but I think the actual

execution in the day to day for all of us working in the trenches, we welcome the support from high above, but I think it is also important that we communicate very closely with the actual sites. So as far as the Air Force participation, one of the reasons we did not include the Air Force during our initial considerations is because their duration for basic training is 6 weeks, and we're looking at studies of 8 weeks duration.

DR. OSTROFF: Thanks. One other comment that I heard you make in the presentation was that there were delays of a couple of weeks that were possibly related to getting results of some of the laboratory assays that needed to be done as part of phase one. Have those challenges or obstacles been overcome.

MR. LIGHTNER : I believe they have. Again, Colonel Sun is as closer to this than I am at this point, but we're still on a course for unblinding the data --

COLONEL SUN: Yes, if I may address that as well. Actually, what it comes down to is, the

specimens that needed further additional testing -- and these are specimens that we identify as adeno but are trying to serotype them -- and because the initial serotyping with PCR did not give us the answer, we're having to amplify some of these cultures for retesting or additional testing with MCRs.

So that's the only thing that accounted for the delay. And we're fully confident that by the end of this month, we should have all those results finalized one way or the other.

DR. OSTROFF: Thanks. I could presume that there were no financial obstacles to getting some of this work done?

MR. LIGHTNER : No. As I said in my summary slide, I think that right now funding is, is good. You know, we could always use more, but we're not in any duress for funding at this moment.

DR. OSTROFF: Great. Let me open it up to other members of the Board. Dr. Oxman?

DR. OXMAN: I'd like to congratulate the

Dr. Ostroff and the members of the Board and all the other people involved in moving this very, very important project forward at flying speed, and I hope that will continue. I have some technical questions to ask, but maybe they would be more important -- better asked on a one on one basis of Dr. Sun. But they involve the question of how the antibody response technically is measured and the issues of the stability of the virus that's shed in the stool.

Dr. Sun, do you want to address either of those issues in the more public forum, or would you rather have an offline discussion?

COLONEL SUN: Whatever suits the Board. Well, the antibody, we are using the colorimetric microneutralization antibody, which is a nicely sculpted (phonetic) format. It's an assay that was adapted from Crawford-Miksza. In our hands we've fully validated it and are confident that this could be the assay -- this should be the assay to use in the pivotal trial.

As far as shedding, we did a the

previous study in 1998 of the Wyeth vaccines. And during that study, in which we only followed stool shedding for 4 weeks, and at the end of 4 weeks we're still seeing 40 percent of the vaccinees shedding adenovirus in their stool. And while we don't know the -- because we haven't broken the code yet, the duration of the stool shedding for the phase one, we're only observing no greater than 28 days, which is an important point for us because we would like to at least be able to say that in the pivotal study, we will not need to monitor stool shedding, because basic training doesn't extend beyond 4 weeks. And we won't really have to be concerned about secondary transmission, you know, beyond 4 weeks.

DR. OSTROFF: Yes. Make sure to identify yourself.

DR. ENNIS: Maybe Colonel Sun could answer this or address this. I would be, as I'm sure you are, concerned about the potential implications of switching from a WI38 to the MRC5 cell substrate, and in terms of regulatory

questions and in terms of the use of data being developed in the clinical studies with the WI38 substrate produced vaccine now and presumably for the rest of this year.

Are there examples -- I know about W -- is this a logical thought to switch from one to other, but it probably will present logistical concerns, I think. And I wonder if there are examples where other vaccines have been licensed or approved and studied clinically that were produced in WI38 -- for example, rubella vaccines years ago -- and then switched to MRC5 for background data?

I think this will be a question that the FDA is likely to ask.

DR. LISS: If I may -- this is Alan Liss again -- I'd take it from our medical expert, Dr. Sun. Certainly you ask very good questions, and we're considering them. One perhaps clarification. Obviously, there are no clinical trials going on right now. That clinical trial was finite, the dosing, and we're now just

recording data.

We are discussing with the FDA and we will continue discussing with the FDA what is necessary to minimize any additional trials due to the cell line switch, if necessary. As well as, everyone should understand that this is not only a development issue, but what we call a manufacturability issue. We have good indication that the MRC5 cell line gives a higher virus yield, which gives more tablets per dose, which gives you a more abundant and -- I hate to say it -- cheaper product.

So all of those factors are being considered, and we're not going to trivially change without everyone weighing in and having the risks and benefits put in. But excellent questions. We are considering them. And if anyone thinks of anything else or questions offline, certainly send them to me. We want to make the right choice at the right time.

DR. OSTROFF: Other comments? I have one last question. I presume in the protocol for

the phase two and the phase three, some of the Board members may recall that there were issues related to the use of this vaccine in females. And is there an assurance that there will be an adequate sample size for female recruits to be able to address this particular concern?

MR. LIGHTNER : Yes, I think we can say that, yeah. That's a factor in almost every clinical study we do now. So it will be looked at.

DR. OSTROFF: Other questions or comments?

If not, we really appreciate your willingness to be here today. I think that I could speak for Dr. Poland in that certainly after my departure, we will make sure that this remains a high priority for the Board to continue to watch very closely the progress, again, to get to where we want to be in 2007. So I can assure you that this won't be the last time, hopefully, that we'll be able to see you or Mr. Howell.

MR. LIGHTNER : Thank you.

DR. OSTROFF: Thanks very much.

Before the break, we have one final presentation, and our next presenter is Colonel Stephen Berte. He's going to talk about chemical and biological medical systems for the advanced development of chem-bio medical countermeasures for DOD. And we appreciate you being here.

COLONEL BERTE: Good afternoon. It is a pleasure to be here to visit with you again. I was here last year, and what I'm going to do is kind of reprise my briefing from last year. I have noticed that some -- if you look in your packets, you'll see that I have moved a lot of kind of background slides into backup, so you still have them to refer to. What I'm going to do is concentrate mostly on our active programs and where do they stand, concentrating on changes since last year. I've demonstrated particular interest to see how things have progressed from year to year. So that is going to be the focus of my presentation today. Let me see.

So here is the agenda. Very briefly,

some organizational information. Talk about our acquisition process. And then we'll talk about the two programs within the CBMS.

This is an acquisition program, so at the top of our chain is the defense acquisition executive, Mr. Wynne. Our line leads through the Army acquisition executive, Mr. Bolton, to Brigadier General Steve Reeves, who is the joint program executive officer for chemical and biological defense. And then he has got seven, soon to be eight, project managers, of which I am one, that work within the chem-bio defense program.

In 2003, when the defense chem-bio implementation program which was put into effect, which was a congressionally mandated program, the implementation plan that went into effect went into what we call the triad, which is the advanced developer which is represented by the JPEO and the JTMs; the requirements office, which is here in the joint requirements office; and the tech basis representative by the joint science and technology

office for chem/biodefense within DTRA.

So we have the requirements tech phase and advance development are the primary triad. Of course, there is oversight of the chem/bio defense program, being Doctors Klein and Schaeffer here, and we have interaction with other staff agencies.

The chem/bio defense program is organized in the systems of systems -- systems of systems approach. And within it we have -- working on a continuum of threats. We have medical products popping in for us early for prophylaxis as well as for treatment, and then there is a number of other systems. We don't rely on just medical systems. We've got individual and collective protection and a number of other program areas: Decon, contamination avoidance, your detectors and so forth.

What CBMS concentrates on are those FDA products. So you see some red crosses out here, but we have nothing to do with medical hospital type systems, protective systems. That is in the collective protection program. It has nothing to

do with FDA. It's strictly tentlike systems and such. So the chem/bio defense program is integrated to assure we provide the best protection to all of the DOD.

So if you look now at that other organization chart, you saw these two charts. As I said, there's eight -- soon to be eight project managers. And within my program shop, there's the joint vaccine acquisition program and the medical identification and treatment program, vaccines and diagnostics and pharmaceuticals and the clinical agents program.

So as I said we're focused on FDA. Our strategy on the requirements, the DOD requirements. We're focused on FDA licensure as our in point. We're looking at every opportunity to leverage other programs, other DOD programs, as well as international partnerships. On the international level, for example, we have under the CBRMOU, which is the Chemical, Biological, and Radiological Memorandum of Understanding between Canada, the U.K. and the U.S., we've got a project

arrangement with Canada on the smallpox system, and out of that we'll end up with a product, with a BIG-IV product that will be licensed in both the U.S. and Canada. We are in the process of having another PA sign on the plate vaccine, and that is a tri-national between the Canada, U.K. and the U.S. to potentially develop that vaccine that will be licensed in all three countries.

The idea behind this approach is to get around the problem of lack of regulatory harmonization. We can do that with these arrangements where we all join together to develop a product, and each country, we share in the cost, but then each country takes on the cost, obviously, of any specific regulatory testing or any testing that needs to be done to meet its specific regulatory standards that don't overlap with other countries. So in the end we can end up with a better inoperability on an international level. But we're also working within the U.S. with other government agencies, and I'll touch on that as we move through.

So obviously we have to move within the President's budget. But what we're doing is spinning our schedules to minimize product development times, and we expand or contract our product line based on the amount of money we have in the pot. In the past couple of years, with the implementation of the plan, there's been a much tighter coordination between advanced development and tech based funding lines. There were some disconnects where we ended up with a product ready to come out the chute to go to advanced development and not having funding ready for it, and we're erasing those red lights with better coordination at the tech based and advanced government level. So at the last comp process (phonetic), we've gotten money in place for the products we anticipate -- for most of the products we anticipate coming down the road.

But as I said, our approach is to minimize schedule. So the way we have aligned our budget is that we do what it takes to get a product out, and what money is left over goes to

the next priority and so on, rather than saying, gee, there are those five or six potential products out there; let's split our money across all of them to try to move them all forward. We don't think that's going to get us across the finish line anytime soon. So we want to concentrate on perhaps fewer products, but products that we know we're going to be able to get licensed or approved.

And this is kind of the metric that we're looking at. We're looking to industry to see, you know, what's the standard? Roughly 6 plus years from clinical to development phase. If you look at what our schedules look like, we're pretty much in the ball park. And we're always looking for ways to shorten our schedules. So that's a constant theme within CBMS, is how to get things out to the war fighter sooner. So that involves working closely with FDA and with our industry partners who are developing and manufacturing these products.

JVAP is, as you know, responsible for

licensed vaccine systems. Here's a summary of where we are, and this you'll recognize from last year. You saw a similar chart. Anthrax vaccine absorbed is in introduction. BIG-IV has been licensed by FDA; that's approximately 6 months ahead of what we were projecting last year when we talked to you. This is the product, the BIG-IV, that Canada is also -- we are also working with Canada to help them get it licensed in their country as well.

Recombinant BOT remains on schedule. We are working serotype AB. DHHS is working on serotype E, among other things, but using the same recombinant system, so that there is the potential down the road that we may end up with a trivalent for DHHS and DOD, with the trivalent rather than just a bivalent vaccine. But AB is ahead of the E effort that DHHS has. We are working very closely with them; we have regular meetings with them, our team and their team. But we're going to continue on with every degree that we need to move on with the bivalent product, because otherwise we'd be

standing still waiting for the E construct to catch up.

Plague vaccine. This year we're projecting that we've cut off a year out here on the licensure. And we've moved here -- here you can see where these -- well, you can see, the licensure moved up. And here, the phase two trials are expected to start here rather than here, which is what we had anticipated last year. So, again, trying to get efficiencies and shorten our schedules.

Now, VEE was below the line last year on funding, but through the recent (inaudible) process and the enhanced planning process that was a part of that, we obtained funding so that the VEE program is now fully funded, which it was not last year. And based on -- we weren't funded; we did have a plan. And right now, we've knocked about a year off of that. But again, always looking to see what we could do about getting fast track status for products, that sort of thing, we've had success in doing that with our vaccine

products.

Medical identification and treatment systems. As I said, there is drugs -- the diagnostics, the Joint Biological Agent Identification and Diagnostic System, JBAIDS, as well as a critical reagents program. The critical reagents program not only developed assays for our diagnostics systems, but they are responsible for developing the assays for all DOD detector systems as well.

We've got several products in production. And this is what the -- we've pulled a couple of items up. The recombinant bioscavenger was below the line last year, as was a radioprotectant. We're projecting that those are going to come in in '06 and '07 respectively. And so we've got a program waiting to be able to transition them. Now, the bioscavenger is even a better example of interagency coordination, I think. That is, the DOD tech base -- in this case, ICE and RAR (phonetic) -- had a plasma derived by a scavenger product, human

butyrylcholinesterase. DOD was looking to recombinant bioscavenger for reasons -- for various reasons, the primary of which was the total life cycle cost that we anticipated. It would be a lot more expensive and a lot harder to get the volumes we need doing a patent-derived method rather than a recombinant method. And this is the product that's being derived from goat milk, so the human protein of this is generated in goat milk, so you can get much better volumes. So that's where our money was, literally.

But due to cooperation with DHHS, between DHHS and DOD, what we came up with was to take the bioscavenger plasma derived by a scavenger product, and dOD is providing funding and we're managing it out to what we would call milestone B, milestone B generally being the point where you start just prior to phase two clinical trials. So DOD is funding phase one, and we're about to let a contract to do that with industry. And then at this point, DHHS is going to pick it up and take it to licensure, we anticipate with

Bioshield funding they will be applying for under the Bioshield program to fund this product and to get it out there.

So we'll get that, and that's going to give us a head start, to have something on the shelf sooner than we would have the recombinant product. The DOD is hoping for the best with this product, because in the long run it's going to be cheaper. And I think in the end, if this product works out, it will probably -- DHHS could well move over to that product too.

It's a good example, too, of the challenges of interagency coordination, because what a lot of people feel is, oh, Bioshield; we should be able to leverage Bioshield for DOD too. Well, that's true if our requirements overlap. Since DOD primarily focuses more on prophylaxis rather than on therapeutics, DHHS tends to take a different approach, the big difference being the different size and types of populations we have. We have a small mobile fit force we're putting in harm's way, whereas DHHS has a whole country to be

thinking about, so they tend to look for solutions that are more along the lines of therapeutics. And so sometimes, even though the agent that we're talking about may be the same, the requirements for the product at the end may be different. So what we need to do is always be alert to know that if we transition something over to DHHS from the DOD perspective, that what comes out at the other end is going to meet our needs. Also, if DOD has a need and the DHHS requirements, those two needs overlap, then DOD should be able to leverage our Bioshield program, because obviously DHHS needs it, and presumably one of the ways to get to the endpoint is for DHHS to develop it with DOD assured that our needs would be met, and then we could just buy through DHHS through the Economy Act.

But those requirements are something we all have to keep in mind, to make sure that what comes -- and in this case, for example, DHHS might be very happy with a bioscavenger product that they've administered to first responders via IV,

because they're thinking, okay, we've got some first responders. There's been an incident. The first responders are coming out of the hospitals, for example. We're going to pump them with the IV, and off they go. Whereas DOD wants nothing to do with IV for soldiers. We're looking more at an IM administration.

So in the end, there's an example of having the same product, but the route of administration could be different enough that our needs may not quite coincide. So it makes it just a little more complicated than at first you may think. But those are the things we're working through, and we're working with DHHS on this program, as well as other programs, so we have to keep all those things in mind.

Okay. Then this is just kind of a look at where we are and where we're going in the next 2 years, projections. As I said, we got BIG-IV license. Plague and VEE programs are moving forward. We expect to be in a phase two trial with the plague candidate, the U.S. plague

candidate, this year. Plasma drive by scavenger, the contract is probably going to be awarded within a week, I would say. We are that close to awarding. We're having milestone B decision for recombinant bot, again, milestone B being the point where we'd be starting phase two after that. And JBAIDS, we're doing low-rate initial production on that system, and expect to have initial operational capability this fiscal year.

And then in FY06, the DOC (phonetic) will continue on with the recombinant bot phase two clinical trial, and recombinant bioscavenger then coming in in '06, as opposed to the plasma-derived product.

JBAIDS block two -- what that does, that adds some toxins rather than just agent diagnostics. And we'll be moving off on that in '06. We're already laying the groundwork to achieve that milestone at the end of '06 this year.

So in closing, we'll remain focused on FDA licensure, working with other agencies and

other countries to try to leverage their assets as well, to not only meet our needs, but to achieve a level of interoperability that might not otherwise be possible. I think it is really important too not to focus entirely -- obviously, because it's my mission -- on advanced development, but the inputs to our program are primarily from MRMC -- the vaccines, obviously, and an awful lot of -- virtually everything coming out of USAMRIID. ICD is involved more on the mid side (phonetic), obviously, and the chemical solutions. And the MID, for example, is also involved in the CRP program, the chemical reagents program, working on the assays. So it is really -- as in any project like this, it has got to be a team effort. And I think we have really a great team in the DOD working between the tech base and advanced development, and I think the teams are developing very well too on the interagency level.

So as I said, I've got other slides in backup if you want to look at them. That is primarily background information. And subject to

your questions, that concludes my presentation today. What are your questions?

DR. OSTROFF: Thank you very much, Colonel Berte. And from my perspective, I have to congratulate you. It sounds like a very refreshing approach to product development and acquisition.

Again, for those members of the Board that haven't been here for long, we have a presentation on JVAP every year. And it's been one of these areas where it's been quite frustrating for the Board, because being able to demonstrate any progress has been a tremendous challenge. And there has been a history from one year to the next of seeing milestones head in the wrong direction and only get longer and longer, with very little product coming out of the end of the pipeline so I have to confess that is really -- it warms my heart to see some truncating of some of the timelines.

But one of the things that I'm hampered with is that most of my materials are still in

boxes between Atlanta and Honolulu. So I don't have last year's milestone charts to be able to compare the information that was presented last year to the information that's being presented this year. And I see where there is some relative shortening of the milestones. But help me understand, when you say 5, 6, 7 years being in line with industry standards, it's my recollection that many of those products have been on those milestone charts for years. And so it's not like we're all of a sudden starting with some of those products.

And my second question would be, you're showing us those that you have prioritized. If I was to take out last year's charts, would I find things that are now longer being shown on those milestone charts? What's been sacrificed in order to accelerate this capability for these products?

COLONEL BERTE: When I prepared those milestone charts, I started out with last year's. And all that we did, really, is to move things up. I think if you go back and look, they're virtually

identical except for those changes that I highlighted with the arrows. Products that were there last year are there this year. They're either above or below the line. So I don't think that -- you know, I would welcome you to dig them out and look at them, but I think they're pretty much the same.

I think in terms of the progress forward, I'm only going to address the here and now. I'm here now. This is where we are today. We put in place, as I reported last year, a new acquisition strategy that I recounted again here that I think is showing that we are making progress with the new strategy of focusing our efforts and our resources.

So all I can say is that we're making progress. When you look at -- the time scale I'm looking at is from initiation of the clinical phases. In a lot these projects, it's arguable whether we got to the point of clinical trials soon enough. But we're there now, and based on what our project plans are, we anticipate that

we're going to move out in pretty good order. I think that we've got a good team. In terms of the vaccines, in particular, our prime systems contractor, DBC, I think is doing a great job. I think that the bringing in of BIG-IV as the first product off the line, and bringing it in a little early compared to what we thought last year, is a good sign. The relationship and the reputation with the FDA continues to grow and improve. I think they're doing a great job for the DOD and we're very pleased with the progress that the whole team is making, not just the contractors, but the folks that I have at CBMS, that's who I think are doing a great job. And that's really the -- the real emphasis is really -- if you want to talk vaccines, because we have a prime systems contractor there, is a team approach. And it truly is a team effort. We are colocated with our prime systems contractor for vaccines, and there is constant up and down flow physically and e-mails and everything else. And the IPTs that the product manager, Lieutenant Colonel Travis

Bernritter has put together, I think is doing an excellent job of ensuring that all the players are involved and we're getting the best product and plans that we can.

DR. OSTROFF: Bob, just let me just reiterate, I have to congratulate you, because this is such a refreshing improvement from the way things were as recently as 2 years ago. You're really to be congratulated in being able to take something that wasn't working very well and evolve it into something that I think, at least speaking for myself, I'm very hopeful will get us to the finish line with some reasonable certainty that we'll actually get there. So I think it's great.

Let me just open it up to other comments from the Board members.

COLONEL BERTE: And it's all to my folks, because they're the ones who are doing all the hard work.

DR. OSTROFF: Yes. Again, Dr. Ennis.

DR. ENNIS: Hi. I enjoyed your presentation. I confess to being overwhelmed by

the amount of data presented this morning. And to a lesser extent by this overview, but this is my first go-around.

Vaccines are a very, very complicated to develop. And I wanted to learn a little bit from you, and I've read about some of the problems with one of these programs on vaccine acquisition. I wanted to ask you to tell us a little bit about the process of review and decisionmaking to put these things online for clinical studies and to go forward. And I don't expect you to do that in detail. But do you have outside peers' advising input, in addition to the contractor and people in the DOD, as part of this process? I'm stepping back and looking at the big picture, not just the here and now.

COLONEL BERTE: I think that a good example of where there is that sort of interaction that I think you're getting at would be -- just one example would be the bot program, where we're working very closely with DHHS and having a sharing of information there where folks -- the

teams from DHHS are looking at our program and we're looking at theirs and moving forward on a unified front.

DR. ENNIS: I was thinking more of the vaccines, the plague vaccine, anthrax vaccine, the process of identifying the candidate and going through the clinical data. Who reviews it, in addition to your team and the contractor -- and the FDA, ultimately?

COLONEL BERTE: Well, it is our program and we are primarily responsible for doing that. When a product is going to transition, of course, there is a joint effort, a team effort between the -- if it comes out of a tech basis, these products have between MRMC and the advanced developers to share information and review the programs and determine whether in fact that product is ready to move forward. And then once it is in advanced development, we've got the technical teams within DOD looking at it. But do we have a routine, in-depth review of each product by an external organization? No, we don't.

DR. OSTROFF: Want to add anything, Terry, to that? Is there any thought being given to possibly to having that type of outside input?

COLONEL BERTE: I think particularly when we're considering bringing new products into the program, that's a time when we are going to be looking at reviews of the potential candidates, for example. As you may recall from the chart, we anticipate to bringing a ricin product forward in FY06 -- at least we've got things set up to do that. And there are a number of products there. USAMRIID has a product, but there are other products beyond the DOD. And so one of the things that we're looking at doing is setting up and thinking about how we're going to have an external review to help us that kind of decision.

And we have had from time to time had external reviews in the past. But whether there is an ongoing -- we don't have a routine thing. We do kind of do it on an as-needed basis. We will have an external review.

DR. OSTROFF: Thanks. Any other

comments or questions?

If not, we're a couple of minutes ahead of schedule, so I will take a break, and let's see if we can return at exactly 3:00 p.m.

(Recess)

DR. OSTROFF: Let's go ahead and try to reconvene. Okay, our last formal presentation, but certainly not least, of the afternoon is an old friend of the Board, and I hope will continue to be an old friend of the Board, Colonel John Grabenstein, who's going to give us an update on MILVAX. And we're looking forward to your presentation. Colonel Grabenstein's handout was passed around. It's the nice colorful one. And just one thing before you get started; I believe Colonel Gibson has a very brief administrative announcement.

COLONEL GIBSON: Through (inaudible), we were able to get 8.25 CME credits for this meeting. To receive the credits, you need to sign the roster, which is outside. It says CME on it. And preferably do that today. And then complete

the evaluation forms; they're right by the door here, on your way out, on the right side. You need to fill out the evaluation forms and turn them in before you leave. We will mail you the CMEs. I don't have the contract support to get them done in between time so we can hand them to you before you leave, but we'll take care of them and mail them to you. Thank you.

DR. OSTROFF: Take it away, John.

COLONEL GRABENSTEIN: Thank you, Dr. Ostroff. Thanks to the members of the Board for the invitation to come back. What I'd like to do today is give you an overview of the key components of the Department of Defense military immunization program. The four words in the subtitle are the four key domains that we focus on as we do our best to keep the troops healthy with vaccines with good science behind them, delivered in a quality way, with care for the service member both during and after vaccination, and with that earning the confidence of the vaccines.

It's been a year now since the U.S.

soldier, meaning U.S. service member, was named Time's person of the year. And I have not entered this on my CV. I don't know about my colleagues in the room. But the point I make is that the real credit goes to the people who are not sleeping next to their spouses at night, not sleeping on mattresses above the floor, and are contending with camel spiders and other interesting ecologic facts of life where they are. These are the people -- these are my customers, or, really, I should say, these are the people I work for, as is true of a great many of you in the room.

This is the menu of military vaccines, or vaccines for service members. I exclude from this list the vaccines for our children. But these are the vaccines that are given, in the lefthand column, universally to all service members or focused in an occupational way or geographic way, and over on the top right are the two vaccines where we are able to vaccinate against bioweapons and provide medical

countermeasures before exposure, and in the lower right, essentially, this being the baseball season, is the on-deck circle. And these are the products we're watching. I'll talk about several of these as we go through this session.

Here's the agenda. This basically breaks down into four quarters. We'll talk about anthrax vaccine, what is new in its science, where we are programmatically, and the legal and regulatory status of the product as of developments yesterday; smallpox vaccine, where we are with it in science and programmatically; flu vaccine, from the standpoint of logistics and policy implications as we look forward to fall 2005; and then the last quarter of the talk will be talking about upcoming vaccines and some other programmatic issues, human factor issues. And adenovirus has already been addressed by Dr. Lightner and Colonel Sun and company.

So we'll start with anthrax vaccine. This is the anthrax.mail website where we -- this is the Christmas tree where we hang all the

ornaments or all the safety studies that we have published, as well as resources for vaccinators and adverse information, and you can sign up for our listserv where we'll give you the news. And the bottom line with the science of anthrax vaccine is that we have more safety data than we have ever had, and we have more longterm safety data than we have ever had. I make this simple point very explicitly because of the continued number of voices who argue to the contrary. And so my second handout at your place is a 44-page summary, a 1- or 2-page summary of each of the safety studies that have been published -- they are each linked to the website as well. Actually, this looks like this is a popular little item and there is no longer any on the back handout table. But the document is available at our website at the resource center button at the top resources button at the next website.

So where we are with the science for anthrax vaccine is that the vaccine still works. That's based on the Brachman study from the 1950s,

based on rhesus monkey experimental inhalational challenge data and rabbit data. And in the FDA's opinion, anthrax vaccine works against all forms of anthrax regardless of route of exposure. We'll talk about those who disagree with that in next slide.

The bottom half of this slide talks about the safety studies. And you've heard me say for many years that there have been 18 safety studies. Well, there now are 20 human safety studies, which have among them 34 peer-reviewed publications, which are the ones summarized in the packet of papers that I gave you. And so the FDA is cognizant of all of them. The National Academy of Sciences is aware of -- or was aware, when it issued its report in 2002 -- of many of them, and there have been additional ones published since. We have ACIP -- Advisory Committee on Immunization Practices -- recommendations for anthrax vaccines, actually, in 2000. And the CDC has provided to the Food and Drug Administration in January interim results from its dose reduction route

change study, which the manufacturer, Bioport, is considering in terms of merit to change the route of administration from subcutaneous to intramuscular, and to change the number of doses in the primary series from six to five. And Bioport is assessing the suitability of that data to present to FDA for a formal change in licensing, which we consider likely to be submitted in the next month or so.

This is a summation of the study titles back when there were 18 studies. I haven't bothered to go out and add the other two, because it would just get less readable as we go. And I think it already makes the point that there is an incredible amount of data about the safety of the vaccine that, in summary, amounts to what the Institute of Medicine said, which is that anthrax vaccine has a safety profile similar to that of other vaccines.

But there are three new studies that I'd like to highlight for you. This one comes from the Assisted Reproduction Technologies Program at

Walter Reed Army Medical Center, where they looked at the effect of anthrax vaccine on sperm. And so the title of the article in Fertility and Sterility gives the conclusion, and that is that the anthrax vaccine does not affect semen parameters, embryo quality, or pregnancy outcome in couples with an anthrax-vaccinated male Service member. This is a single-cohort study where it was the cohorted men going to this fertility clinic, 254 of them anthrax-vaccinated, 791 of them unvaccinated, over several years. It's self-reported vaccination for institutional -- for reasons related to institutional review board processes. But the two groups were found to have similar concentrations of sperm and semen, similar in terms of sperm motility and morphology, the need for intracytoplasmic sperm injection, rate of fertilization of ovocytes, embryo transfer and also at late pregnancy. And indeed, the diagnosis of male factor infertility was less common proportionately in anthrax-vaccinated men than unvaccinated men. The only vaccine I know that

has gone to this level of study.

One of the persistent accusations against anthrax vaccine is that there is no longer safety data about this vaccine. That is not true. And the next two slides will show you how there is indeed more longterm safety data on anthrax vaccine than any other vaccine, I believe. This is a study from the journal of Occupational and Environmental Medicine, looking at soldiers who had received one or more doses of anthrax vaccine from 1998 to 2000. The Army has all of its disability discharge evaluations computerized, so we were able to create one cohort of vaccinated soldiers and compare them to a couple of unvaccinated soldiers. And they were followed for 4-1/4 years using Cox Proportional Hazards models for risk of evaluation. Not the finding of the disability discharge, but the evaluation of disability, and then the ultimate outcome of the granting of the discharge as well. And the adjusted hazard ratio is .96. The unadjusted rates were 140 per 100,000 person-months if

unvaccinated; 68 per 100,000 person-months if vaccinated. And obviously, because anthrax vaccine has been, one might say, a travel vaccine if you're going to Southeast Asia or Korea at various times, there are selection biases that might apply, so the statistical adjustment was quite important.

But looking at separate adjusted hazard ratios just for men, just for women, just for permanent disability, for temporary disability, just musculoskeletal, just neurologic, each of those subgroup separate analyses were -- or stratified analyses -- similarly shows no evaluated hazard ratios. And one of the issues the authors consciously took into account is issues of latency, that there may be a period of time that's needed to elapse between vaccination and manifestation, and that was not seen either.

And so the conclusion is that anthrax vaccination does not change your risk disability evaluation, nor granting of disability finding as the outcome.

And then the other new study in terms of longterm safety comes from Colonel Pittman's group here at USAMRIID, following up 155 Fort Detrick alumni who worked here as lab workers from the '40s to '60s. They received a medium of 154 vaccinations or skin tests during their average 17 years of employment. That's considerably above what their civilian colleagues would get. Ninety-two percent of that 155 received anthrax vaccine. And the data collected came up through -- I believe much of the blood samples were collected at a picnic, an alumni picnic in 1996. They were studied from first vaccination to -- well, the interval of following any individual workers ranged from 15 to 55 years with a mean of 43, and their mean age was 69. And they were contrasted with 265 community controls from this area matched on age, ethnicity, and gender. The lab workers did report fatigue statistically more than often than controls did, but that fatigue was not associated with the number of injections, number of vaccines, or time in the

program. Perhaps more importantly, there was no differences in self-reported medical outcomes, medical conditions in the group. They did find some laboratory anomalies in terms of monoclonus spikes or paraprotein peaks. They were statically elevated, but there was no association there with lifestyle, vaccination, or medical conditions. And so the conclusion is that intensive vaccination is not associated with an elevated risk of disease or medical condition.

So this slide is mine -- as a program manager, I have a responsibility to tell you the following: That there has been some very vigorous assertions that the Department of Defense is withholding information from you, withholding information from the public about the lack of safety of anthrax vaccine, and smallpox vaccine and other things as well, but principally about anthrax vaccine. This is not idle internet chatter. This is filings with the Food and Drug Administration, filings with the U.S. District Court, a spoken interview on WTBD television in

Durham, North Carolina. And so I tell you this and -- partially, one of the ironic pieces of this is that much of it implicates me personally as me withholding information from you.

So I tell you this so that your due diligence is to make sure that information is not passing you by, that we aren't rubber-stamping or whitewashing or passing over key details. And so I would suggest that if at any point you feel you are not getting the information you need or want, that you please inform one of the surgeons general, inform Ms. Embrey, or inform Dr. Winkenwerder so that we can remedy that situation.

Now, the programmatic piece to the anthrax vaccination program is as follows: We are at full stop. A judge for U.S. District Court for the District of Columbia imposed a complete injunction on anthrax vaccinations by the Department of Defense and the Department of Health and Human Services on the 27th of October. Between the start of our contemporary program in March of '98 and that injunction, we had given 5.2

million doses to roughly 1.3 million Service members and city workers. From a supply standpoint, Bioport is doing just fine; they were producing steadily, and the inventory is accumulating, because we're not consuming.

What is the legal situation? The judge has deemed in his ruling that anthrax vaccine is not indicated for inhalation anthrax, because the Food and Drug Administration in a 1985 -- excuse me, in a 2004 action did not have a 90-day commentary, public commentary. So the judge essentially threw out that January '04 final rule by the FDA, remanded it back to the agency for the lack of that public comment period. That public comment period opened at the end of December. It runs for 90 days, which expires on the 29th of March. So you have 7 more days to provide to the Food and Drug Administration any comments any of you as individuals might wish, or the Board as a whole, to the FDA about what your opinions are about the anthrax vaccine. About one hundred people have done so already. And so that's where

that piece of it stands.

Now, when the judge made his ruling, we were left without an ability to deliver anthrax vaccine to keep the troops healthy and protect them against bioweapons. So the Department of Defense requested and then the FDA ultimately issued an emergency use authorization, an EUA, which is a relatively new regulatory form of permission to use a drug product that came about -- simplifying, but came about by means of the Project Bioshield Act. This is an emergency authorization for anthrax vaccine used in a six-dose series for pre-exposure protection which the FDA granted on the 27th of January. We have been unable to act on that EUA because the injunction enjoins it. And so the Department of Justice lawyers have gone back to the judge from the U.S. District Court for the District of Columbia requesting that he modify the injunction that was filed the 14th of February, if I recall. The judge set a hearing for yesterday. At the hearing yesterday, the judge heard arguments from

Plaintiff and Defendants, and has elected to think about it for another 12 days. And so the two parties will be going back to the judge on the 1st of April to hear what the judge has to say. If the judge doesn't demodify the injunction, then we would resume the (inaudible) under emergency use authorization pending the FDA's action to close out the comment period and for FDA to reach its independent decision on what to do about the license status of anthrax vaccine. So in other words, the public comment period ends on the 29th of March, but that's when the last envelopes are received, and then the FDA has to deal with the documents submitted to them.

And on this point, one last point here that I'll make is that we have -- it was briefly touched on this morning -- we have an additional document to request an emergency use authorization for a three-dose anthrax vaccination, post exposure. This came of interest, of course, last week with the anthrax alarms in the federal buildings in and around the Pentagon. And that

use of that product would also have been encumbered by the injunction. So this is rather tangled, and I thought if, with the chair's and indulgence, because of the sheer complexities of each of these segments, that I would stop and take fact-based questions. This is the end of the anthrax section. I'll take the anthrax questions now, and I'll take smallpox questions later, and if that -- Dr. Ostroff, as you wish.

DR. OSTROFF: That's fine with me. Let me open it up. Dr. Brown.

DR. BROWN: Mark Brown. It seems to me that, you know, there's a group of people who are going to be concerned about the anthrax vaccine that you're never going to convince with any data. But I'm wondering. It seems like some of the publications that you cited there looked, I don't know, pretty convincing to me. You're really looking at -- for example, looking at sperm function or integrity or whatever, or something. It looks a little bit farfetched on one hand, but I'm sure certain Service members are worried about

something like that, so I think it is a legitimate thing to look at.

I'm wondering if you have any plans to take all that data and do some kind of appropriate outreach to everybody else out there. You know, there's a group you're never going convince, but there's everybody else. It seems like you have almost an obligation, I would argue, to take that information now and in some form disseminate it to people who have concerns.

COLONEL GRABENSTEIN: Yes, and you're absolutely right. In 1999 and 1998, we were caught. We thought we had a very sophisticated educational program, more sophisticated than we had ever implemented before. And it was overwhelmed by a vaccine skepticism that knocked us back on our heels a bit in '99, even up through 2000. And so we have been doing a tremendous outreach program to the Service members involved.

And in my opinion, based on what we've seen -- for example, in calendar year 2004, we administered this vaccine to essentially

100,000 -- excuse me, essentially one million people in calendar '04 itself, with well over a million doses. So our impression from talking to Service members, talking to unit commanders, is that there is general understanding of the need for the vaccine. Certainly the anthrax attacks of fall '01 made the threat very concrete. And so it is the rumor control and making sure that the new people in the system are aware of and understand, you know, why it is that the dedicated scientists who have read all the literature keep recommending the vaccine.

DR. BROWN: Well, if I could just follow it up, it seems like you have all the ammunition, you know. You've just got to go out and use it.

COLONEL GRABENSTEIN: Yes.

DR. OSTROFF: Can you give us some idea of, at this point, with this approximate 6-month gap, what proportion of personnel that are deployed to what are considered to be higher-risk areas are not adequately or at all protected?

COLONEL GRABENSTEIN: I'll be a bit

vague, because it discusses vulnerabilities, but fundamentally one fifth of the people at greatest risk have received no anthrax vaccinations whatsoever. Of the other four fifths -- well let's do quintile. So 20 percent, no shots whatsoever. Sixty percent are behind schedule, because we haven't been able to vaccinate them. And then one fifth are on schedule, not yet due a dose. And so we are increasingly uncomfortable with vulnerabilities that we face.

DR. OSTROFF: Then the second part of my question would be, obviously you're going to have a significant catch-up need, once you are able to resume the vaccination program, particularly in deployed areas. Do you have thoughts or strategies about how you're going to be able to accomplish that?

COLONEL GRABENSTEIN: The catch up issues. Yes, it will be -- when the injunction came on, our dropoff in vaccinations looked like Niagara Falls in terms of the rapidity with which we stopped vaccinations. When we resume, it will

be stairstepped back up. So I don't have an estimate at this point, you know, about how many weeks or months it will take us to get back up to a steady state again. But it's going to be, you know, restarting the locomotive.

DR. POLAND: Greg Poland. Two things. One, John, just, again, a congratulations. This is a marvelous program and information resource. I don't think there is anybody who seriously looks at the issue of anthrax vaccine that doesn't come to this website, because it is almost the holder of all information there.

The second comments is one of the PIs of the CDC study. It may be important for the Board just to recognize that this is a study being done on civilians, 1,560 of them who will get the full series of immunizations, and it's a double-blind, randomized, and importantly, placebo-controlled trial on immunogenicity. The results of that trial are reviewed by FDA and by yet another independent board of experts that form a DMSV who review this quarterly. We're more than halfway

through the trial, and suffice it to say the trial continues. There have been no significant safety concerns identified in this cohort.

DR. OSTROFF: Yes.

MAJOR SMITH: Sir, this is Major Randy Smith, joint staff. Could you mention briefly for the Board's benefit the right of refusal issue that's associated with the EUA?

COLONEL GRABENSTEIN: Right. The Emergency Use Authorization is section 534, I think of the Food, Drug, and Cosmetics Act. It was put there by the Project Bioshield Act. And it allows for an option to refuse, is the term within the regulation. And so we would be implementing -- so if the injunction is modified, we would be implementing the EUA with an option to refuse. The EUA -- our intent at this point is to resume it within -- principally within higher threat areas, principally CENTCOM Korea. And so there will be a need for expanded information, a challenge even greater than what we've confronted before, about which we -- you know, we know how

smart Service members are, and we know that they understand risk and they understand other vaccines they've gotten. So we're designing educational products to take under account.

DR. OSTROFF: Other comments or questions?

I'll just point out -- before I turn to Dr. Gray, I'll point out for the Board members that we do have a draft of a submission to the docket regarding the federal rule being put out by FDA. And when we break in executive session we'll have further discussions about that.

Dr. Gray?

DR. GRAY: Greg Gray here. John, we were made aware of some proposed legislation that would make both receipt of anthrax and smallpox vaccines voluntary. I wonder if you would care to comment regarding how you think how such a law would impact the programs.

COLONEL GRABENSTEIN: What is unique about military culture and military society is the teamwork involved, and it is a mutually dependent

team, so that if any individual member in the team is lost, the survival of the other team members on the battlefield or in the battle space is less.

So that is the reason that military vaccinations are mandatory. It's because if I decline a vaccine or vaccination, I can make you less likely to come home safe. And I don't have the right, to deprive you of that privilege. It is a conflict between individual rights and group rights or group responsibilities, but it is one that the United States military has followed for many, many decades.

And so with all respect to the congressman who introduced the bill, I personally would respectfully disagree with it, and I believe that is the position of the Services back to the U.S. Congress in terms of our recommendations to the Congress on how to act on the bill.

DR. OSTROFF: Thanks. Why don't you move on to our next topic?

COLONEL GRABENSTEIN: Smallpox.mil, same format. The three pivotal buttons are here,

adverse event info, information toolkit, and resource center. They were over on the right margin on the anthrax site.

This is what I call the box score of where we are with the smallpox vaccinations. We started on December 16, 2002. We have now screened something like 830,000 people. We vaccinated about 768,000 of them. Roughly two thirds primary vaccinees, given their age distribution. Roughly 88 percent male and 12 percent female.

Our exemption process is working well. We've had zero cases of eczema vaccinatum, zero cases of progressive vaccinia. Our education process is working well. We know we can always do better. And we sometimes need to tap people on the shoulder to make sure they are listening in the classes they go to. But we've had roughly 79 cases of autoinoculation out of the 768 -- that's one per ten thousand, so that's not too bad. Contact transfer of vaccinia, 53 cases still predominately bed partners, spouses, and adult

girlfriends. It's the guys giving it to the girls. And sports partners -- there are a few Marines on Okinawa and other cases. So this pattern here caused us to revise our education materials to say, don't let your guard down at home, which was where the risk was. It was not in trip units, in hospitals, in clinics. We still are at zero transmissions from vaccinated patients to health care workers or health care workers to patient. We've had 250, more or less, women vaccinated when we did not realize they were pregnant, and of them, about 75 percent, they conceived after vaccination, or they were such a little bit pregnant -- they had so recently become pregnant that no test would have detected it. And so that's 75 percent. That means 25 percent we might have detected, and so we reinforce the need for screening in a candid way, so that the woman can be frank with the people in the immunization clinic.

I neglected to say earlier -- I should say it now -- congratulations to CBMS, JVAP, and

Dynport for the licensing of vaccinia immunoglobulin intravenous in February, as Colonel Berte mentioned. We have modeled as we began that we would need BIG about 1 per 10,000 vaccinations, which means we should have used it about 77 times by now. We used it three times, and I think I've talked with you about these cases before -- I don't think there was anybody new here -- one burn patient and two ocular patients. One case of encephalitis in about the second month of the program and none since. The surprise was the myocarditis and periocarditis cases; the count is now 94 -- 81 probable, principally on enzymes, 4 biopsy confirmed. Seven deaths following smallpox vaccination. Six unrelated, according to civilian advisory committees. One possibly associated. That's the 22-year-old reservist we've talked about on previous occasions. And this is a summary from 1,611 VARES reports and other reports to headquarters.

Now, we've been updating you as we've been going with our efforts to understand the

carditis more fully, and this is where we stand with the registry. Eighty-seven of the 94 have had a full review from cardiology by now, and you see the percentages there. These are principally white men in their 20s, primary vaccinees. And onset symptoms -- this cluster is in the second week after vaccination -- manifest with elevated enzymes, abnormal ECGs, and sometimes abnormal epicardiograms and (inaudible) occlusion on cath, typically. We have now followed -- well, about 20 percent on follow-up report that they had some residual symptoms. One of those cases is persistent migraines in a prior migraine recipient. But mainly the bulk of it is a chest discomfort -- not chest pain per se, not in the ischemic sense, but what we've chosen to describe as chest discomfort -- that dissipates over time. And so you see it at 3 percent in the second 6 months after vaccination. I'll talk about the MRI and the white blood cell scans shortly.

We recognize our challenges to be keeping the clinicians aware that they should be

looking for it if someone presents with chest pains in the ER, to be thinking carditis and not just musculoskeletal. And we are intrigued by this discomfort issue, and I'll show you more data as we go, and working to make sure that many places that we vaccinate have resources they need to do these follow-ups. We are flying people long distances to get these cardiology reviews, as I'm sure you can imagine.

This is what I refer to as the Washington Monument graph. This is the clustering of myocarditis cases in the second week after vaccination. And this is the ejection fractions of day of diagnosis, which you see rapidly in return to the 60 percent level in terms of returning to normality.

And this is created exercise stress test. This is -- unit is mets, which I think is a composite unit of many variables -- but 10 is considered normal. The couch potato people are down here. And this is a well-performing function. And so an 8-minute mile is here, and

that's 10-minute miles down here, so, in high-endurance athletes. So this is recovery after -- this is carditis patients after recovery. Nobody is down here, which is really remarkable.

Now this is a reverse Kaplan-Meyer plot of recovery. This is based on date of examination, so it is pessimistic that the recovery could actually have occurred over here, but we didn't find out about it until over here. But red is ejection fraction, green is electrocardiogram, and then blue is chest discomfort, yellow is any symptom, so the difference between the blue and yellow is the migraine guy. But this is the 20 percent and the 3 percent that I talked about earlier that we are continuing to pursue. And this is written up in the Journal of the American College of Cardiology.

So what can we say about that 3 percent, that 20 percent of residual chest discomfort? The cardiologist have adapted magnetic resonance imaging and indium-labeled white blood cell scans to go look at them in greater detail. And these

two summaries are just posters presented to the American College of Cardiology last week. And if any of you are into nuclear medicine scans or MRIs, you can -- I didn't bring my magnifying glass, but you're take a look at this after we break. But this is that data. Very succinctly, but, 33 of the patients have been worked up with MRI studies, 22 of whom were persistent chest discomfort patients, followed out a considerable length of time after vaccination; 10 show some inflammation persisting a year after vaccination via this assay. Now, one of three with two sequential assays shows resolution 2 years later. None in this -- the last line may be the most important of those bullets -- none show evidence of scar formation in their heart.

Now, my Professor Savitz from UNC is surely sitting over there scolding me for mixing short-term and longterm followup patients in these rows. But that's what the cardiologist gave me. I don't have any better way to look at it. We'll get it stratified and we'll show you the

(inaudible) as well.

Nuclear medicine scans, white blood cells, looking for inflammation again: 12 patients, 19 scans; 9 of the 12 had persistent discomfort, long durations after vaccination. Seven had inflammation. Of the five who were symptom free, none had inflammation, and maybe this is the most important of them: None had fixed profusion defects in areas of healing inflammation.

So what does this mean? We don't have a good control group yet. And I was intrigued to find out that carditis cases are not serially followed in the civilian sector, so there isn't a whole lot of information about what to expect and so the diagnostic, prognostic, and maybe more importantly, therapeutic value of these data aren't clear yet; maybe it's useful for evaluating people who present late. Maybe it's to look for abnormalities. Now, remember, even these anomalies are in people who are exercising at the levels -- you know, the high performance exercise

levels that I showed on the graph. So this is -- you know, the cardiologists let me use an analogy that we dumped a bunch of water on the campfire, but there is still a glowing ember. Maybe that's what this is, maybe not. But without a control group with carditis symptom-free and healthy, never having myocarditis, are needed to really understand what these data mean.

So with regard to cardiac conditions after smallpox vaccination, there are three main findings. We plead guilty with regard to causality for myocarditis, periocarditis, principally known as white men, young white men. And as you know from I guess it was last spring's presentation, we had been following four cases of dilated cardiomyopathy. There are no new cases, even though we have continued to vaccinate. I had one member from one of our advisory panels say to me, well, that means -- if there are no new cases, that means the vaccine did it. And I said, no, I think that there are no new cases; that means the vaccine didn't do it. But you can tell me your

opinion, because you're the Epidemiological Board.

So my word is probably not guilty, or in the ACIP/AFEB working group's words, they remain neutral on the subject. And then with regard to ischemia, the smallpox vaccination caused heart attacks. The military evidence is clearer than ever that the regular heart attack in the ischemic disease is the same as in smallpox vaccinated and unvaccinated groups. Data not shown, but we're about to submit -- we just had a new manuscript we're about to submit for publication pointing that out, and we've provided that to the Board members, the working Board members. The stance for the civilian population is quote, unquote "neutral."

So Dr. Poland, Dr. Gray, Dr. Gardner, et cetera, are on the ACIP/AFEB smallpox vaccine safety working group. That group is nearing completion of its report of 640,000 vaccinees worth, I think, combined civilian and military programs. There is a separate neurologic events report that is nearing completion, and the

sentinel case review process we have talked with you about earlier at previous meetings -- that's where the 22-year-old death case was, for example, is nearing completion as well in terms of submission to journals for publication.

So that's the end of the smallpox block, so I'd offer an opportunity for comments, again.

DR. OSTROFF: Well, let me again congratulate you. This is a phenomenal effort. And keeping all this information up to date with the scope that you do is really a monumental task. And so congratulations to not only you, but to the staff that worked with you in putting this together.

Let me open it up to the working group members, if they have any comments, and then I'll open it up to the general group.

DR. LEMASTERS: Grace LeMasters. I was just wondering, under the perivaccination during pregnancy, what was the number, the total number? It was 75 percent undetectable, but --

COLONEL GRABENSTEIN: It's roughly 250.

Commander Ryan, am I right there?

COMMANDER RYAN: Closer to 300.

COLONEL GRABENSTEIN: Three hundred.

DR. LEMASTERS: And has this changed at all? I mean, what was it last spring?

COLONEL GRABENSTEIN: We looked at it as a function over time, and it's been relatively steady. The women slipping through the cracks have been slipping through the cracks at a constant rate, essentially.

DR. LEMASTERS: Well, we talked about, you know, perhaps changing a question as I recall last time to having unprotected intercourse in last 30 days. Did we make any changes to decrease that number?

COLONEL GRABENSTEIN: The form was changed. You may know -- I don't know that we have it at that level of granularity. I'm sorry to put you on the spot. Commander Ryan runs the smallpox registry at the Naval Research Center in San Diego.

COMMANDER RYAN: The form was changed to

be more clear about pregnancy screening in terms of last normal menses. So it does not ask still about intercourse, but it does ask about the date of the last normal menses, because we were seeing women who slip through who said their last periods were normal and on time, but without providing the date. Normal and on time is not what we would consider clinically nonproblematic. So with the date in there, more women have gotten screened a little more closely.

I did see -- the most recent case who presented to the registry unfortunately was screened with the old form, and likely would have been captured with the new form. Now, the rate, that 75 percent, does look pretty steady over time. But I anecdotally will tell you that the new form does a better job of not letting women slip through.

COLONEL GRABENSTEIN: So when we found that out, we were putting together a push to make sure that we assure that the proper form is being used.

DR. SHANAHAN: The only thing I wanted to say is that at first, I was upset when you called the ten-minute miles debilitated. Just for the record. Nobody deteriorated to that degree.

The question I had, actually, though, was in the carditis and the myocarditis and pericarditis -- I didn't, maybe, catch that. Were there predictors of who was susceptible to that among the -- in other words, I mean, you focus a lot on the sort of consequences. But I was just curious if there was any sign of who was most likely to suffer that particular complication.

COLONEL GRABENSTEIN: We looked for body mass index. We looked for smoking. We looked for a variety of things early on. And the only thing we came up with was being a white male.

And so the Naval Health Research Center is going to do a case control study taking the cases, matching them with the controls, and going looking at risk factors to see if there is something more refined that we could use as a predictor.

DR. OSTROFF: Right. And in addition, being a primary vaccinee?

COLONEL GRABENSTEIN: Right. That's right. Year. Of the 94 cases -- I don't know the percentage number in front of me, but I think it's 2 or 3 of them are revaccinated, so the disproportion is marked.

DR. OSTROFF: Dr. Gardner?

DR. GARDNER: Just to follow up on a little conversation I had with John a little bit ago, the new concern, of course, here is the myopericarditis and the issue of are we going to -- what are the longterm consequences? And everything looks quite reassuring -- mostly reassuring. Ten percent after a year is still not entirely reassuring with evidence of inflammation, but still pretty good. And their function tests look pretty good.

I don't think we'll ever satisfy for a very long time the issue of whether there might be some late consequence of the fibrosis or some sort of late term sequelae. And John reminded me that

the first real study of myocarditis was done in the Finnish military, where they prospectively looked at them, I think, for 30 days and found a 3 percent incidence of EKG changes. This was done a number of years ago.

COLONEL GRABENSTEIN: In the '60s.

DR. GARDNER: It would be very interesting to go to Finland and see what happened to those folks 30 years later, whether there were any differences, because I don't think we'll ever lay this issue to rest. At 5 years they'll say, well, what about 10 years? At 10 years, what about 15 years.

And that Finnish population, the Scandinavians, keep good records, and you might be able to really identify who those folks were. And that would be very important data in terms of trying to answer some of the longterm issues.

COLONEL GRABENSTEIN: The suggestion to go look at the Finnish data came in from Major Schry (phonetic), one of the cardiologists at Brook Army Medical Center. And so, Ms. Embrey, we

may come to you for some -- the international collaboration part is easy, but we may need some money. But if we can accelerate gaining the knowledge, I think we should, because it has programmatic and policy implications.

DR. OSTROFF: Dr. Brown. Certainly if you're going to do it, go in summer.

DR. BROWN: Mark Brown. On a completely nonmedical issue, has the smallpox vaccination program run into anything like the kind of opposition or resistance that it seems that the anthrax -- it seems like there might be some comparisons or contrasts you could --

COLONEL GRABENSTEIN: Yes, the contrast is extraordinary. The smallpox vaccine is a live virus vaccine that causes events that were widely publicized in the brochures from the CDC, in pictures that looked just awful, and scared a lot of people away from the vaccine in the civilian sector. And it rolled out in our population smooth as silk. And I don't why -- I mean, I don't know how to attribute our good fortune with

regard to the smallpox vaccination program, because the level of effort for smallpox was akin to our current contemporary level of effort for anthrax.

And so -- I told people that what I do is 10 percent immunology and 90 percent sociology, and I'm still trying to figure it out.

DR. OSTROFF: John, one last question before we get to the third part of your presentation. I assume that there are no supply problems right now in terms of availability of vaccine? And are there any thoughts about how and when there might be a transition to the large amount of ACAM2000 that's been acquired by HHS?

COLONEL GRABENSTEIN: Right now we're drawing off essentially the CDC's longstanding late '70s, early '80s production of Dryvax, the original -- the traditional vaccine used in the United States. We are drawing on it. We purchased it from CDC and are reimbursing them for their costs.

We are drawing down that stockpile at a

fairly slow rate. There is still plenty to draw from. And the potency keeps getting retested and keeps passing, and we're still able to continue using the product with assurance of potency.

With regard to the alternate product, ACAM2000 from Acambis, as I think we have talked with you before in the session, ACAM2000 was also associated with myocarditis: Some symptomatic cases, some asymptomatic cases. If you just look at the symptomatic cases, it's a higher frequency, though a better-monitored population, but at a higher frequency than we've seen with Dryvax, which would then lead us into the policy dilemma of, do we shift to the products produced in a pristine cell culture base that may have a higher rate of carditis, and which has been in a grand total of -- I'm not sure of how many, but maybe 20,000 people, as opposed to a product that has been almost a million people in the last year, last couple of years, but in tens of millions, maybe hundreds of millions of Americans in the twentieth century? So that would be the policy

dilemma.

DR. OSTROFF: Thank you very much. I'm going to move on to the -- oh, I'm sorry. Dr. Oxman.

DR. OXMAN: Mike Oxman. Just a question about, do you have information both on the Acambis product and this product, and also different preparations of the Dryvax on the ratio of antigen to infectivity? Because one of the things that has affected the side effects, if you will, of vaccines that is not well recognized is when you improve the vaccine lot so it has a higher yield of infectivity to antigen, that's not always a good thing.

COLONEL GRABENSTEIN: As you can see with varicella, I believe. That's right. The other thing confounding the dilemma I just described was, we know that Dryvax works in terms of preventing infection and preventing variola infection and improving or reducing disease rates. And whereas the ACAM is studied serologically and immunogenically and not in a true

infection-and-prevention manner -- not true efficacy.

So no, I don't know of an antigen -- I guess it would be really living to total viron (phonetic) would be the measure you're describing, right?

DR. OXMAN: Right, because it may be that cardiac effect, if they're related, may reflect viremia, and viremia may actually be greater with a tissue culture vaccine which probably has a higher titre of virus related to antigen than Dryvax.

COLONEL GRABENSTEIN: We've mounted greater efforts to assess viremia serologically in throat swabs, et cetera, with Dryvax, and essentially we're zero out of a big number in terms of retrieving virus with Dryvax. I don't know what the viremia data is with ACAM, so I'll look around the room to see if anybody, any of the usual suspects, might know that answer. I don't know. But we'll check into that.

DR. OSTROFF: Thanks. Let me offer two

options. One of them is, I mean, you've been up there for almost an hour, and we could take a brief 5-minute break and give you a breather. Or if your preference is just to get through the last component, I'm open to that as well. I'll open it up to the Board for their preferences.

COLONEL GRABENSTEIN: I'm fine. It's up to you all, in terms of a stretch.

DR. OSTROFF: Carry on.

COLONEL GRABENSTEIN: Charge on. All right.

Influenza, from Camp Funston, Kansas, 1918. I would point out to you the mortality effect of World War Two, which is somewhere in here, I think. Oh, there's this other big thing over here that you've noticed. That's one of my favorite graphs: Life expectancy and the outrageous or extraordinary decline in the 1918 experience, which many of you have read in depth.

So in the 1940s the Surgeon General of the United States Army commissioned this Board to go invent or refine or develop -- I'm not sure

precisely what verb to use -- an influenza vaccine. So the Army and the Epidemiological Board's predecessor have great claim to the value -- or providing an influenza vaccine to the nation. To the world, basically. So we have for many, many decades had a universal influenza vaccination policy, which was rolling right along until October 6, I think, something like that, of 2004, when Chiron announced that it would not be shipping influenza vaccines to the United States. And so DOD had purchased roughly 3.8 million doses, or ordered it. And then when Chiron -- and two thirds of that was to go to Chiron's Fluviron. So we ended up with one third of our expected quantity of flu vaccine. So we were grateful to Sanofi Pasteur for allowing us to purchase more Fluzone from them, and then we also went to MedImmune to buy FluMist from them.

So we went from our traditional universal vaccination policy for service members to a targeted one. The very first shipments of injectable vaccine we got went to Korea or went to

CENTCOM -- went to Iraq, and then Afghanistan, and then to Korea. And then it was -- first crack at the vaccine went to the troops deploying to those locations.

From our beneficiary standpoint, from the family members and the retirees, we went from a policy of broadly encouraged to a targeted one that matched the Advisory Committee on Immunization Practices in terms of, what, five or eight categories based on medical risk and age and what have you.

So we encouraged the herbicists (phonetic) to purchase FluMist instead of FluZone, to free up the FluZone for those people who could only receive the injectable product. We assisted the states by not buying 200,000 doses of the injectable product that we intended to buy so that it could be purchased in your communities. And our communications efforts stressed intervention and calm and handwashing and all that kind of stuff. And we figured at the beginning that we'd have enough vaccine to just sweep by our reduced

adjusted requirements.

So Colonel Phillips and Ms. Embrey were intimately involved with our interim policy, then our final policy, then our revised policy, then our updated policy, and then our the-last-one-on-this-chart policy -- five different memos as things kept changing. That's what I've said previously, so I'm not going through each of those. But in the end, the behavior of the beneficiary group was the same as on the civilian side: People said, oh, my mother needs it more than I do, or give it to my neighbor, and they didn't come in, the people who didn't want to come in to get vaccinated -- very altruistic on their part, but we had vaccine waiting for them. And so in the civilian sector, we will throw away vaccine this year because we couldn't find any takers for it.

And one of the key lessons, I think, from my perspective is, you can't make your policy too fancy, and you can't change it too often. You've got to kind of stick with it. We really

ratcheted down in late October, early November, and then people didn't come in, and so we've been backpedaling ever since.

This was our first big use of FluMist, so these are some of our findings. Pardon me; you have to start with logistics. It's shipped on dry ice, which meant that it was shipped to the lower 48 -- we finally convinced MedImmune that Alaska and Hawaii were part of the Union. That's a little bit too cavalier, but -- we were unable to convince certain aircraft pilots to let dry ice -- somehow dry ice is dangerous and explosive; ammunition isn't. I don't understand that, but great reluctance to put dry ice on a military aircraft. But the pragmatic piece of this is, it's bulky. And so the normal freezer in an immunization clinic could hold maybe a 2-day supply at their normal rate of consumption, or in the really busy clinics, a half a day supply. So that was a major issue. Then eventually MedImmune worked it out with FDA so we didn't have to use the freeze boxes, but we also had to throw it away

on the 8th of February, and so it was a tradeoff.

On the consumer side, there was -- remarkable to me, after our success with the live virus smallpox vaccine, great angst that the FluMist contains a live virus. That took some talking through, and some people never got talked through it. And there was the perception that various postvaccination side effects were due to this funny vaccine that we gave. And I went myself to one of our immunization clinics and sat around in the anaphylaxis waiting room and talked with Service members after they had been vaccinated, and they kind of had this deer-in-the-headlights look about them as they were processing the fluid through their nose. So, you know, there are some human factors to this. And here is the sociology piece. We all think, oh, wouldn't it be great to avoid the needle? But receiving that needle is a learned behavior, and our folks have learned it, and they haven't learned, here, show me your nose, let me stick this up it.

So the other pragmatic part was that the package insert was hyperconservative with respect to simultaneous vaccination. It basically did not permit inactivated vaccines within 14 days or live vaccines within 30 days of FluMist use. And so we confront one of these on-label, off-label, "if you go off-label it must be researched" conundrums. And so we implemented FluMist abiding by the package insert, even though the ACIP said, aw, go ahead and give it, you know; if you're going to give, you know -- the standard rule for lives vaccines is, don't worry about if it's an inactivated vaccine either simultaneous or 30 days apart if it's two live vaccines. MedImmune did go back to FDA and receive permission Friday, I think, to revise the package inserts. And so the package insert of FluMist now reflects the ACIP recommendations. And so that constraint is no longer with us, but that held us up through the fall.

We buy flu vaccine with last year's money. We buy with -- FY04 funds expire on fiscal

New Year's eve, the 30th of September. That's the money that's used to buy the '04/'05 flu vaccine. So we suddenly had a change in policy and a change in product, and we had no money -- you know, the '05 money was reserved for this coming September. So fortunately we were grateful to Defense Supply Center of Philadelphia for reassigning the '04 money to the alternate national stock number to let us, let the hospitals and clinics buy FluMist with the previous year's -- what amounted to the previous year's money.

So come September, we get to do it again. And two points. Our surveillance program for natural, normal, everyday, run of the mill usual flu, not to mention pandemic flu, is as solid as ever. I'll keep going and when I finish, then I'll -- I think we'll have a separate talk about Project Gargle, and if anyone wants to make any comment to Ms. Embrey about purchases of antivirals for DOD or the federal government --

We had a summit meeting here at Detrick a couple of weeks ago when we were dealing with

anthrax alarms in my office building to talk about flu policy for this coming fall. It's clear that price per dose matters. This troubles me from -- I understand the budget dilemmas at the local hospital and clinic level. But we are in a case where if somebody doesn't support MedImmune, we're going to lose the manufacturer of a product that has certain advantages.

We are still uncertain about what Chiron's status is. They seem to be doing well where the British government has given them permission to proceed. Whether that means any of the lots they manufacture will be released or not remains to be seen. So, but we need to plan if a shortage were to repeat. If it were, we would probably repeat the prioritization scheme for '04, but loosen it up, given our experience with people stepping aside to let others be vaccinated who didn't show up either.

We had several clinics with catastrophic refrigerator or freezer failures, to their regret, and so we need more alarm systems. And then I'll

close with an issue with a few slides that I plagiarized from Dr. Poland. We in the Army are considering whether -- how to encourage vaccination, influenza vaccination, of health care workers. And let's see -- these are the slides I stole from Greg. The issue of health care workers with symptomatic and asymptomatic spreading virus to their patients is a patient safety issue, not to mention the economic issue, you know, or the cost benefit to the employer of keeping the worker on the job, and especially with critical nursing shortages. A statistic of something like 70 percent of health care workers work despite being ill, because we're important, you know, and they need us. And so we're going to go take the influenza virus to them while we're working. And an article from Clinical Infectious Diseases about the transmission of influenza within health care settings. And so at the moment, the national average is something like a third of health care workers are vaccinated and two thirds are not, and that's a problem which we intend to address.

So Steve, anything on antivirals you wanted to add?

LIEUTENANT COLONEL PHILLIPS: Just a couple of pointers. I'm sorry, this is Colonel Phillips.

On the issue of flu vaccination policy for next year, if I could say something about that first, one of the things we worked out at the summit meeting that we had last week is that, taking into account the planning factors of the things that we know and the things that we think we know about what the supply is going to be next year, we are planning on doing -- resuming total force vaccination.

Last year we went from total force to targeted with the deployed and deployers because of the shortage. This year, we said we've got some advanced warning. We know that Adventis is in; Chiron may or may not be in; GSK may get in late as far as TIB. And so what we need to do when the service representatives are here, as I said, is we need to plan on the worst case

scenario, best case scenario, and what level of risk the Services are willing to accept in terms of the supply there.

One of the decision points for us in terms of our policy points next year will be, in April we'll find out from Sanofi Pasteur how much FluZone they're willing to sell us next year. And as Colonel Grabenstein pointed out, price per dose does matter, and the Services are leaning toward using -- utilizing TID as much as possible, because it's less expensive than the LAIV FluMist product, though they all recognize that FluMist would be required to a degree.

And so with the general principle of, we are going to do the total force; we're going to try and keep the price down the best we can; there's some risk involved in saying we're not going use the more expensive LAIV, and take a chance that Chiron or GSK will be in, the Services are going to get their orders in here within about a month based on those principles.

So there's a lot of planning and a lot

of analysis going into developing what we're going to be doing for next year with that.

DR. OSTROFF: Thanks. I have a couple of comments. One is that you have to factor in in terms some of what Colonel Grabenstein presented in people stepping aside, et cetera. It wasn't entirely altruism. It's the fact that we just fortunately had a very mild flu season. And not only was it a very mild flu season, it was a very late flu season. I don't think that we can count on that happening next year. And so I wouldn't discount the desire of large proportions of the beneficiaries to get that vaccine next year.

I also don't think it's a good idea to introduce risk, because as we know from lots and lots of experience, you can be penny-wise and dollar-foolish. And I would strongly urge -- and I think the Board would be supportive of this -- to diversify your acquisition base to the degree that you can, because you can't count on, as we saw last year, any of these particular producers necessarily coming through in the way that you

think that they're going to come through. And so I would strongly encourage to the degree that you can that make sure that you have a diversified acquisition base. And setting aside the issue of trying to support MedImmune, it just makes a lot of sense to me to try to do that to the degree that you possibly can.

LIEUTENANT COLONEL PHILLIPS: This is Colonel Phillips again. That was one of the principles that we talked about, is having more than a single supplier. We can't buy all our 3-1/2 million doses from Sanofi, because there's awful lot of risk if you put all your eggs in the one basket. But if you diversify too much and you say, well, let's get, you know, the 1.4 from Sanofi, but let's count on getting a half million from GSK, and, you know, 2 million from Chiron, there's risk involved in that as well, because we don't know if they're going to be in the market for sure yet or not.

DR. OSTROFF: Yeah, but if they're not, then you've got less vulnerability in terms of not

having an adequate supply. And I just -- there's so many variables, as we know, in terms of flu vaccine that I just wouldn't count out any potential option.

I think that Dr. Lemasters had her hand up, and then Dr. Poland.

DR. LEMASTERS: This is really a sidebar question maybe more for you, Dr. Ostroff. I was reading an article about the place where influenza is breeding is in the school age children, and they're getting it and passing it around to their family members and they're bringing it home. And if we inoculated children, then we might just stop or really drastically decrease the flu epidemics that occur. I just wondered if anything is being done?

And I was just thinking, in communities where we're deploying, also, a lot of our soldiers, maybe that group at least should be targeted for community access to school age children.

DR. OSTROFF: Right. Let me -- I could

ask either Dr. Poland or Dr. Gray to comment on that. I think what you're referring to is a study that came out from our colleagues at NIH that suggested that vaccinating children was more cost-effective or more beneficial than vaccinating the populations that are currently being vaccinated. And I think most of us that looked at that study would not have not quite made the same conclusions. Our conclusion would be, yes, there is definitely benefit to vaccinating school age children, but it shouldn't be at the expense of vaccinating the high-risk individuals which are currently being vaccinated.

Certainly in the perfect world, one would like to see the entire population vaccinated against influenza, because that's the best way that we have available to us to reduce the overall mortality and morbidity from the flu. But if you're going to target populations, I think most would feel that it's still appropriate to target those who have the highest risk of having complications.

And I will would open that up to Greg, to the two Gregs, to make any additional comments.

DR. GRAY: This is Greg Gray. Regarding the collecting some of the young adults versus the children, I can think of two examples that make me think with caution about that. One, of course, is the 1918 pandemic, where the mortality rate was much greater in young adults. But the second was just the phenomenal outbreak we saw when a new emergent H3N2 hit the USS Arkansas, and I think they had 99 percent who had received the annual vaccine appropriately some 2 weeks before. But the ship limped back into San Diego Harbor. The CO, the XO, the navigator -- all with a incapacitating headaches.

And I think that's the reason, particularly, this Board needs to really stand up and advocate for our young healthy population. This influenza can really decimate a fighting population.

DR. POLAND: This is Greg Poland. There is a lot of evidence for that. The Tecumseh

studies in Michigan in the 1950s, the country of Japan instituted that as a policy. And it works if you can get nearly everybody, and if there's not a lot of in-and-out mobility in those societies, probably none of which is the case today.

John, a question for you is, this issue -- and actually, the Arkansas incident might be one of them. This issue immunizing health care workers. The one group of individuals around whom the most vulnerable congregate -- you know, there was one case on the USS Arkansas, they go to sick call, and then the technicians, the nurses, and the doctors get it and spread it to everybody there on in.

Where are we with that, particularly in requiring -- short of, you know, some medical contraindication -- requiring this for health care workers in the military?

COLONEL GRABENSTEIN: We made a draft policy within -- that's circulating within the Army Surgeon General's office. And with all of

the other events in the last month or two, because we don't need it in place until September, it's gone by the wayside. But it will take -- you know, we've got union negotiation. If it is approved conceptually -- there are human factors issues in terms of unions and employee groups of one sort or another. So we want health care workers to value vaccination, the influence of vaccination for its own merits.

DR. OSTROFF: At least the DOD part, I'd love to see that come to the Board.

COMMANDER LUDWIG: This is Sharon Ludwig. I would just like to add to the issue of health care workers and kind of piggyback on Dr. Lemasters's point that we might want to add child care workers to that group of health care workers. I know anecdotally in our child development center at Coast Guard Headquarters, it was not required of the workers. And there was a week where they had 7 out of 12 or 8 out of 12 of the child care workers out sick. And I believe it was influenza. You know, I don't have any laboratory tests, but

the symptoms -- and the children were all sick. And that included my son, by the way.

But anyway, I would just like to add that that is also a vulnerable population -- also, that these children take it home to their active-duty parents.

DR. OSTROFF: Other comments?

COLONEL GRABENSTEIN: Okay, part four. This is the lightning round, for those of you who remember the Match Game.

DR. OSTROFF: In this one, we'll go through the rest of them and then we'll make comments.

COLONEL GRABENSTEIN: Right. Okay. So the Food and Drug Administration recently licensed Menactra to Sanofi Pasteuri, the protein-conjugated form of meningococcal vaccine which has its origins back at the Walter Reed Institute of Research. It was licensed in January. We presume it has a superior duration of protection, because of what we know of this technical approach. The actually clinical trial

date is only 4 years lapsed. So it will be a few more years until we can -- till Sanofi can, excuse me, establish that as a fact. ACIP just adopted a recommendation for vaccination for 11-year-olds, 15-year-olds, and the continuation-with-college-student recommendations. The Joint Preventive Medicine Policy Group recommended to the Services that they substitute Menactra for MedImmune as soon as possible. The ASAP is in lower case there intentionally; it's not rush out and do it, it's begin to work it into your routine plans, again, when the MedImmune is going to be phased out eventually after it gains wider age group licensure.

Menactra is not yet available to DOD. My understanding is that Sanofi is going to ship to civilian customers first, and has assured us of an adequate supply of MedImmune in the interim. This vaccine is given intramuscularly rather than -- Menactra is IM as opposed to subcutaneous for MedImmune, and is liquid rather than freeze-dried. And I've got the AFEB comment at

the bottom of the next few, but I'll drive on.

The other one that is next likely to come up out of the pipeline is Tdap, which is an acellular pertussis vaccine combined with tetanus, diphtheria, and acellular antigens. So if you're not familiar with the nomenclature in the system, it's a capital T because it's -- the same amount of tetanus toxoid is given to infants; it's a lower case D because it's a reduced amount of diphtheria toxoid; and it's a lower case A and P, because it's a reduced dose of pertussis antigen relative to the DPT given to America's children.

There are two brands of vaccine that are in advanced trials, one from Sanofi, one from GlaxoSmithKline, one with four pertussis antigens, one with three; one which is expected to be licensed -- the company is seeking licensure for a broader range, from 11 to 54 years of age, as opposed to 10 to 18 for the Boosterix product as we understand it at this point. Half an ml for both, aluminum adjuvant for both. Presumably it would come to ACIP for its commentary that

presumably would be given for the routine adolescent dose at around age 11 and then the routine booster doses. I've had discussions with Dr. Gardner regarding, what do we know about the persistence of the pertussis immunogenicity, and what would be -- you know, would this be recommended out all the way to 70-year-olds and 80-year-olds and 90-year-olds, or should it be more targeted?

And the other thing is that I just got a TD booster about a year ago. Does that mean I have to wait 9 years before I can get a dose of this? Do we want to bring it up in any shorter interval of time? That's what we will need to get grappled with.

How much pertussis disease there is a never ending question, because it is so hard to diagnose serologically, or in a confirmed manner, I'll say. One set of statistics I pulled was that pertussis in adults, there was an attack rate for prolonged cough illness between 1/2 and 1-1/2 percent per year. Many people at the ACIP meeting

were telling stories about close relatives who had pertussis. And so whatever that number is, that's the direct benefit. And there is the indirect benefit of vaccinating adults to keep the bacteria away from children -- an indirect benefit.

The Vaccine-Related Biologic Products Advisory Committee to the FDA recommended licensure a week or two ago. And the line in Las Vegas is that licensure might come in September of '05. I don't know how much the price differential will be; I don't know what ACIP is going to say. So what will DOD do? Would we phase it in? Would we adopt an absolute change abruptly? I was doing an literature review and I came across this article from Clinical Infectious Diseases by this fellow named Gardner from the State University of New York at Sunnybrook where the subtitle of the article is "The Case for Selective Rather Than Universal Recommendations." So Pierce might enlighten us on his thoughts on that when we get around to this at the question point.

This is the one I expect the most

interesting discussion related to, and that's the next product likely to come out of the pipeline, which is papillomavirus vaccines. Again, two products -- Gardisil from Merck, Cervarix from Glaxo. The Merck product is quadravalent, aluminum-adjuvanted. It is intended for both genders eventually, although it is unclear whether they will seek licensure for women only or for both genders initially, at a dosing schedule of 0, 2, and 6 months.

The Glaxo product is bivalent with an adjuvant called ASO4, adjuvant system 4, which is a combination of aluminum and monophosphorolipid A. They will seek licensure for women on a 0 and 6-month schedule. A fascinating discussion about the differential morbidity and mortality. This is a virus that burdens women far more than men, and yet men are the factors to women -- again, a case of indirect value. Papillomavirus is the cause of cervical dysplasia and cervical cancer, something like 400,000 cases per year and a quarter of a million deaths per year in the United States, and

genital warts. Don't know price, don't know what the ACIP is going to do. What do we do? Would we vaccinate women and not men? Would we vaccinate women and not men if it was licensed for both genders? Would we just vaccinate just for recruits coming in? Would we vaccinate up until age 30? You know, this would be an hour's worth of comments unto itself.

Japanese encephalitis vaccine. Beacon is phasing out its production, its current production line that it markets through Sanofi Pasteur. The Services have funded purchase of JE vaccine via the ACIP with a supply -- I believe this is the correct number -- it should be sufficient through FY10, which is something like 275,000 doses at $17 million. There is a cell culture -- one or more cell culture based vaccines are expected to be licensed in Japan, and hopefully one or more of them will be FDA-licensed by then. And so if you wish to comment on that, we'd be happy to talk about that. I don't have any other.

This is our generic website, www.vaccines.mil, which if you go to the vaccines/diseases button, you get a pulldown menu that lists all of the FDA-licensed vaccines and some of the others in advanced clinical trials as a resource.

One of the -- where we are putting our focus this year is in quality -- quality assurance, quality improvement. I'll go back to the four subtitles I had on my title slide. And we have got great resources that we are working on getting fully disseminated in terms of education of both the professionals and the paraprofessionals involved in our immunization enterprise. It is remarkable, in this era of so many people traveling overseas so often, we need to be extremely professional in the immunizations we deliver. Quality consists of education to vaccinees, ample time to do well, ample time to listen to them when we screen them for contraindications, good injection technique, good culturing management, good recordkeeping, and good

followup.

This is the website from the Vaccine Health Care Center with a project they call Project Immune Readiness, which is web-delivered education, 50 seat hours of medical education credit, nursing education credit, and a few other flavors of -- I think physician's assistant and maybe a few other professions, health professions, in CE credit. And we intend to continue expanding these offerings as we go.

This is the immunization toolkit that the Vaccine Health Care Center assembled that they distribute to shot-givers, and it has been very well received.

We come to the sociologic issues, and on my bad days, I console myself with thinking that Edward Jenner was ridiculed, and things haven't changed all that much. It would be nice to go back to when vaccines were fun. This is Elvis getting a polio vaccine in the '50s. But people don't like getting sharp, pointy objects stuck in their arm. This is Doc asking Sgt. Snorkel,

"Which arm do you want it in?" And he grabs Beetle Bailey's arm and proposes that one.

So we have come a long way from what folks like my father recognized as the shots that he got in World War Two. I was looking through his shot record the other day and realizing that he had gotten typhus vaccine. We have a population that is extremely smart, that goes out and seeks out information, and we need to respect them and give them the answers that they can use.

Part of quality is in good care. That's good education, clinical excellence, making sure at sick call they're asking about previous vaccinations, reinforcing all that we do with VARS (phonetic), keeping an open mind -- who would have thought that smallpox vaccine caused myocarditis? DOD caught it. DOD found it. And to those who say that we have our head in the sand and ignore our vaccinees, that is proof positive to the contrary. On the other hand, we know how to separate mirage from reality. And we were able to show that heart attacks were not due to smallpox

vaccination.

The Vaccine Health Care Centers Network has been doing excellent work in case management, in education, in resource building, in patient consultation, question answering, and they really get kudos for all that they've accomplished.

We have had out for several years now clinical guidelines for managing adverse events after any vaccination, and that's a website that you see there. And our policy is that if medically you shouldn't get vaccinated, you won't. And we should do a good job in finding the exemptions that are clinically warranted.

These are the points of contact for my agency, the Military Vaccine Agency. The Duty Vaccine Clinical Call Center is a 24/7 essentially nurse-staffed hotline that can patch people through to an allergist on call or a physician to get clinical questions answered. The BAC contact numbers, the CDC contact numbers. And then we will occasionally vaccinate a Reservist on a weekend drill or a Guardsman on a weekend drill,

and they go home and 2 or 3 days later have an adverse event, and they're no longer near -- if they're in West Virginia, they're not near an active duty military medical facility, so this is a way to get them support for civilian medical care that they might need.

So where are we going? Quality improvement, quality assurance is the big thing. I am beginning to bring together a bunch of the pieces of what we have been doing for quite some time into something that I'm referring to under the rubric of Immunization University. And it's the combination of all the different kinds of education and training we do. Its clinic-level quality assurance in terms of the competencies of the vaccinators, and then a self-assessment program for the clinic. Principally, I'm envisioning this as something that the NCOICs -- the noncommissioned officers, the chiefs -- can conduct themselves to make sure that they're performing best practices, and we can then do it in a coached way if need be.

And so this is a matrix I tried to put together myself of, okay, if I'm the chancellor of Immunization University, then we have a School of Immunization Science and Care -- that's the clinical stuff, that's the academics, that's the content. And then we have an Academy of Clinical Ops and Quality, and that's the paraprofessional world, that's the fulfillment part, making sure that the SOPS are in place and the E4 vaccinator knows what to do, what not to do, and has sent it to me, signed off on a competency sheet, and we run short-term programs and thinking of it as Shots Are Us. We have, you know, resources available to them working on vaccinator-patient relationships to make sure that they know how to ask a woman candidly if she's pregnant or might be pregnant or wants to get a pregnancy test, or does it in a respectful way so that we get a good answer and are able to do right by our people. And the last row is called Inquiry -- that's research, it's clinical investigation, it's evaluation of readiness in a variety of different

ways. And we need a registrar. We need to know where the physical rooms are where we give shots, and we need to have a phone book of all the vaccinators. And they need transcripts somehow, some way, of what training they've had and how we know that they're ready to do an excellent job and delivering the vaccines that have FDA licenses. So this is still very fluid, that they have drafted Board letters on it. But it's kind of where I'd like to focus in the coming year.

So what we see is important -- how we define excellence in immunization, I think it would be having reliable science. We just can't have the studies in our file cabinets; we have to have it out in the peer reviewed literature. We need to keep our eyes and ears open. I think myocarditis is the example of that. We need to give the shots with quality, exempt people from vaccination when it's appropriate, use the right vaccine and store them well and document it. And then good care while vaccinating, while screening, at sick call. And it doesn't matter whether the

vaccine caused an adverse event or not from the individual perspective. We have a duty to provide care. That's the bottom line. It doesn't matter whether the vaccine was guilty or not in terms of care giving. Then from a science standpoint, we need to go figure out the causality, and we do.

And with those three points, then, we get, I think, to earn the confidence of the troops and their families based on us all working together to keep them healthy and on the job.

And I haven't figured out whether this is four or two or three of them -- we would prefer to do this in the building with a computer nearby so we can enter it into electronic immunization tracking system, but this is what has been passed on to us in long traditions from our fathers and our mothers.

So that, I'll stop and see what questions you might have.

DR. OSTROFF: Colonel Grabenstein, thank you very much for a very comprehensive and, as usual, an outstanding presentation. All I can say

as somebody who is departing the Board is that you alone are worth the price of admission. I'm happy to come back at any future time and hear updates from you.

So let me open it up to Board members and see if they have any comments about any of the other issues that you raised.

Dr. Gray?

DR. GRAY: John, outstanding presentation, real provocative. I'm wondering if the giffenpigs (phonetic) still exist, and assuming that this other pertussis vaccine is approved as John has suggested, if you folks have deliberated regarding what your decision process will be? I mean, the data that I'm familiar with, as far as our trainee risk, are probably 10 years old. And what we're seeing in the civilian community would suggest that there's an increasing risk in our young adult populations. And I'm sort of wondering how you would develop that white paper to defend employment of any vaccine, and which date you would base it upon?

I recalled Cherry out of UCLA published a paper about 10 years ago looking at freshmen in college using serology, culture, and maybe molecular application. I think he had a figure of 24 or 26 percent showing evidence. And I remember we collaborated with the FDA 10 years ago and found even in 2 months of training, we found about half of that. So there is significant morbidity out there, and it is probably increasing. I was just wondering what data you might have.

COLONEL GRABENSTEIN: Jimpig (phonetic) is -- we've not presented to Jimpig yet, and -- just haven't gotten to it yet. Jim Terry presented it in great depth at ACIP. And the numbers obviously hinted -- now, whether you're talking about serological evidence of infection as opposed to disease, to start. And, Pierce, I'll bow to your -- you're the master of the subject.

DR. GARDNER: Yeah, I think you have to be really careful of those serologic diagnoses. Almost all of those are not culture or PCR confirmed.

There is a strong -- there is a conundrum. It's said that, A, there is no such real thing as asymptomatic pertussis; you have to get a cough. But in fact that's -- I think that's up for debate.

I think the military will certainly -- should go to the acellular pertussis DT product. And it would be very nice to know a little bit more about the frequency of pertussis by either serologic studies or others. I'm going to guess, since we know that the teens and young adults are what seem to be carrying the epidemic in young folks, it would make perfectly good sense to do that among the military.

Where I have my problems is that in adult and civilian life, almost nobody gets immunized for anything between about age 20 and 50. If there is a Td recommendation, it is very poorly implemented. The majority of people at age 50 don't have antibodies to tetanus or diphtheria. In spite of the fact that we've done such a poor job, we have zero to one case of diphtheria a year

in the United States, and less than 35 cases of tetanus, almost all which have occurred in people who have never been immunized in the first place.

So just following the data, you could make a very strong case for actually diminishing the every-10-year adult recommendation to say that people who have been fully immunized as children are in an extraordinarily good age group; reimmunize them at age fifty and you're set for life. The data certainly strongly suggests that. The last time I looked at the figures, there had not been a death in the United States from tetanus for anybody who had been fully immunized since 1978 or something like that.

Now, the problem with the pertussis vaccine is the antibodies drop like a rock. So 2 years out, it is hard to measure them. You don't know what the clinical protection is, but -- say you've got a 30-year benefit from Td, but you've only got a couple of year benefit -- perhaps the (inaudible) will be shorter.

And finally, the real group you're

trying to protect with pertussis, where we know the data, is the young adults, and particularly the young parents who may give it to their infants who then bear the risk of severe morbidity and mortality. Our current system really deals with influenza and meningococcal vaccine at age 50 or more -- and we don't immunize very well in that young group. So there is a feasibility and sort of a disconnect.

Finally, since I talked to Greg last night, if you have an outbreak of pertussis, you'd like to have it a monovalent (inaudible) pertussis available to give to anybody, because if somebody had had a Td booster a year ago, you want to avoid the artifice (phonetic) reaction.

So pediatricians complain that the internists treat kids like all little adults. In this case, the pediatricians are trying to get the internists to treat everybody with the whole spectrum of the disease, when in fact the proven problems are mainly among young adults, and again, there's the disconnect between the systems we now

have -- you have to implement a much more effective young adult vaccine system and carry it on the back of pertussis. And that's going to be a little bit of a tough sell, since it's not etched in the high priority in most adult care givers' minds.

DR. OSTROFF: Thanks. Dr. Lednar?

DR. LEDNAR: Wayne Lednar. I would be interested in the comment to this potential concern that I have. It's a first readiness concern.

To the extent that the total force concept involves the Reserves from the National Guard in a major way, many of whom live in communities across the United States -- that's fact number one.

Fact number two is, since many employers are finding it more and more difficult to continue offering employer paid health benefits, more and more people are working for employers where they are not getting health benefits. Unless they are poor enough to qualify Medicaid, they may be in

this medically underinsured or medically uninsured situation. So we may have in communities where much of our activated force may be derived, increasingly, vulnerability to vaccine-preventable diseases.

So I'm wondering how we are going to sort of monitor the extent to which we have in fact an increasing risk that's slowly beginning to emerge. It's kind of a structural consequence of what's happening in front of us.

COLONEL GRABENSTEIN: Well, since we don't provide routine health care for Guard and Reserve folks at home, we don't have access to the data. All our principal inpatient/outpatient medical surveillance systems are active duty-based. So we would rely on -- to the extent that what you said is true, then it would be apparent to the state health department. It's just it would be happening to our people within the state.

DR. LEDNAR: I guess the one (phonetic) to me says it would be apparent to the state

health departments is, in reality for them, it is a very fragile public health system.

COLONEL GRABENSTEIN: Understood. Yeah. You're right. And it would be apparent at the state level if you had the data.

DR. EMBREY: I'll comment on that. This is Ellen Embrey. We are concerned that we do not have very good civilian health data on our reservists, and we are seeking ways now to identify more proactive ways of getting that information without violating their privacy per se. This is in line with increasing the overall readiness of reservists and having a better understanding of their health status before they deploy.

In addition to that, Congress is increasingly providing benefits to the Guard and Reserve with not only access to not only DOD force service, but also to the VA for veterans of combat operations. So we may in fact in the next several years have much better data because of the work of Congress and our taxpayer dollars.

DR. OSTROFF: Dr. Ennis?

DR. ENNIS: I was interested on your update on Japanese encephalitis, and I've heard that the present producer is losing interest. And I see that perhaps there will be a cell culture-derived vaccine available around the year 10.

Do you foresee the coming storm in the sense of an absence, a potential absence, of this very, very important vaccine?

COLONEL GRABENSTEIN: That's why we're buying the stockpiles, to bridge us over until such time -- to bridge us between when manufacturing ceases and when the estimate is when the new products will be licensed. So there is a gamble on several new levels here, but this is our best risk management strategy to tide us over.

LIEUTENANT COLONEL PHILLIPS: This is Colonel Philips. Again, if I could comment on that as well.

We learned very painfully the lessons of the adenovirus vaccine, and then we lost that, and

how long it's taken us to get it back. It was actually actions from this Board a year ago to Dr. Winkenwerder saying, you got to make sure you've got enough of a stockpile to cover you through a very conservative -- as in how long it would take for a new vaccine -- and also telling DOD and Dr. Winkenwerder and the department has also become more aggressive, and that we're not just sitting back and waiting for a new vaccine to be developed. But the folks here from MRMC and some of the researchers from the departments that you heard from this morning are actively involved with the pharmaceutical companies that -- I think there is three of them -- that are working toward developing a new JE vaccine, and monitoring their progress and staying on top of that ball so that we don't get behind the curve on that.

COLONEL GRABENSTEIN: And then following up on that some of the pertussis comments, we will have one of our folks put together an information paper on what we believe in as the most reliable stance in terms of pertussis infection, pertussis

disease in our age populations. And I'll take it to the Jimpig (phonetic) and bring it to you all as well for comments.

I'm curious if you have any thoughts as for as papillomavirus?

DR. OSTROFF: Well, I was going to raise that same question and ask Dr. Gaydos, who I see sitting along the wall, or any of the experts on the Board on reproductive health issues whether they have any thoughts about that particular issue. And then we're going to have to cut off the discussion so that we can get to our executive session.

DR. GAYDOS: This is Joel Gaydos, the Department of Defense Global Emerging Infections.

I think with regard to the papillomavirus, I'm not prepared to address that now, John. But we haven't had many studies of papillomavirus in military women. We've had the Army using the Cytek system, so we should have some data out there that we can take a look at to see what's happening when they are coming into the

Service. And I think it's also going to be important to see how the vaccine is going to be used in civilian populations.

If I may, I had a question, two questions for you, John. With regard to the meningococcal vaccine, and switching from the polysaccharide to the conjugate, do you know if Sanofi is going to provide the data necessary to make a decision about boosting, and also with regard to boosting someone with a conjugate who's received a polysaccharide or vice versa, if that may occur?

The second thing I want to ask is what is the status now of the hepatitis B immunization of all recruits?

COLONEL GRABENSTEIN: I did ask Sanofi about when they would have the data. What I was told was that the main groups for clinical trials got vaccinated 4 or maybe 5 years ago, and so in a year or two they'll go -- they may well be doing annual serologies on them to watch the antibody decline curves. But in a year or two, they'll be

at the a 5-year point, and the data will be gained in real time as we proceed. And I guess we can assume that you don't need a booster until informed otherwise, because the other cohort is 4 or 5 years ahead of where our folks will be.

I didn't ask about the Menime (phonetic) in first, Menactra second question, but I can't imagine that it would be -- I mean, I would be surprised if it was not effective. But since it's a one-dose series, you can just think of it as starting first with Menactra too, I guess would be another way of doing it.

On the hep B vaccination policy, essentially -- I've not asked, but the policy is, all recruits get it, or all recruits are screened and those who are seronegative get it. I don't know anything to the contrary. So I believe that's in place at all 10 of the Armed Forces basic training centers.

DR. OSTROFF: Thanks very much, and again, thanks for such a terrific presentation. I know it went considerably longer that we

anticipated, but there was certainly a lot of terrific information there. So we really appreciate that.

Let me suggest that we take a 5-minute break and then the Board will come back and meet in executive session. And I will promise that we will finish in 30 minutes.

(Recess)

(Whereupon, at 5:05 p.m., the OPEN SESSION was adjourned and the Board continued in EXECUTIVE SESSION.)

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